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4-562

ACCESS DB # 221705

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/13/07

Art Unit: 1624 Phone Number: 2- 0663 Serial Number: 10511537 D

Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: MG

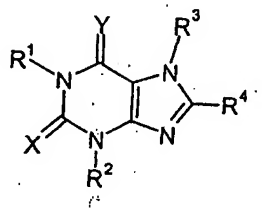
Inventors (please provide full names): _____

Earliest Priority Date: _____ Search #4 +

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



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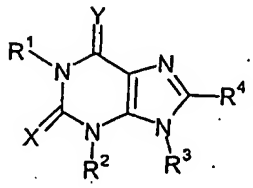
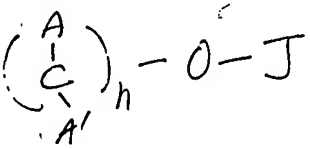


(Ia) (Ib)

X = S Y = O

A, A', R1, R3, R4 = H / CH3

R2 = 

J = CH3 / C2H5

20070412-10511537-set4

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STAFF USE ONLY

Searcher: BOB

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 4-12-07

Searcher Prep & Review Time: 20

Online Time: 11

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

2 Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

55 STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial ____ Oligomer ____ Score/Length

____ Interference ____ SPDI ____ Encode/Transl

_____ Other (specify)

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=> fil reg; d stat que l27; fil capl; s l27
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STRUCTURE FILE UPDATES:   11 APR 2007  HIGHEST RN 929721-97-1
DICTIONARY FILE UPDATES:  11 APR 2007  HIGHEST RN 929721-97-1

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on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1                STR
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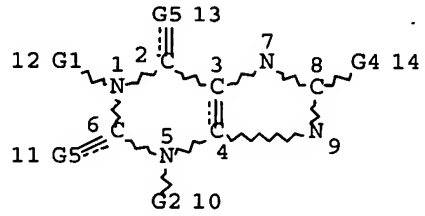

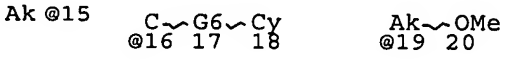

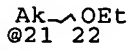


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VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
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CONNECT IS E1  RC AT  15
CONNECT IS E2  RC AT  19
CONNECT IS E2  RC AT  21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22
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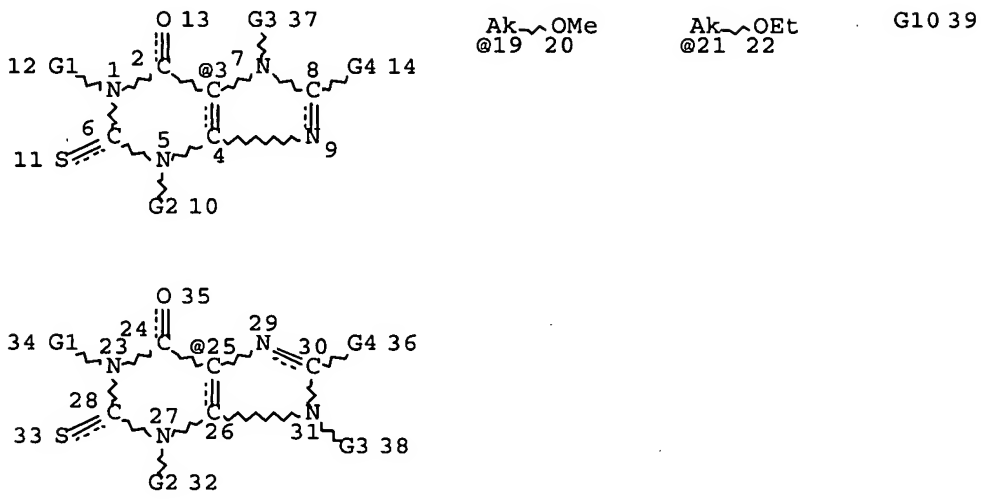
STEREO ATTRIBUTES: NONE
L4 17287 SEA FILE=REGISTRY SSS FUL L1
L24 STR



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CONNECT IS E2 RC AT 19
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
L27 2 SEA FILE=REGISTRY SUB=L4 SSS FUL L24

100.0% PROCESSED 229 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 16:46:53 ON 12 APR 2007

FILE COVERS 1907 - 12 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L28 1 L27

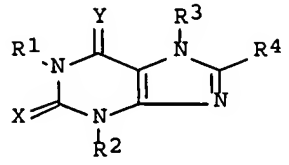
=> d ibib ed abs hitstr l28; fil hom

L28 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089430	A1	20031030	WO 2003-SE617	20030415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480452	A1	20031030	CA 2003-2480452	20030415
AU 2003224548	A1	20031103	AU 2003-224548	20030415
EP 1499613	A1	20050126	EP 2003-721211	20030415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009012	A	20050201	BR 2003-9012	20030415
CN 1646531	A	20050727	CN 2003-808355	20030415
JP 2005526836	T	20050908	JP 2003-586151	20030415
NZ 535406	A	20060831	NZ 2003-535406	20030415
ZA 2004007815	A	20051004	ZA 2004-7815	20040928
US 2005234036	A1	20051020	US 2004-511537	20041015
NO 2004004998	A	20050118	NO 2004-4998	20041117
PRIORITY APPLN. INFO.:			SE 2002-1193 A	20020419

SE 2002-2239 A 20020717
WO 2003-SE617 W 20030415

OTHER SOURCE(S): MARPAT 139:350580
ED Entered STN: 31 Oct 2003
GI



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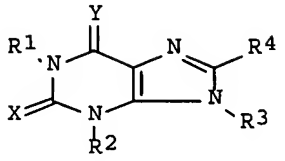
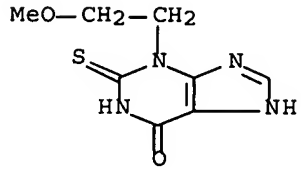


II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μM.

IT **618913-25-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-25-0 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(2-methoxyethyl)-2-thioxo- (9CI) (CA INDEX NAME)



IT **618913-21-6P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-21-6 CAPLUS
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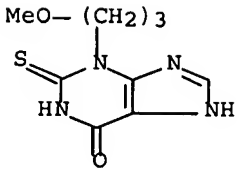
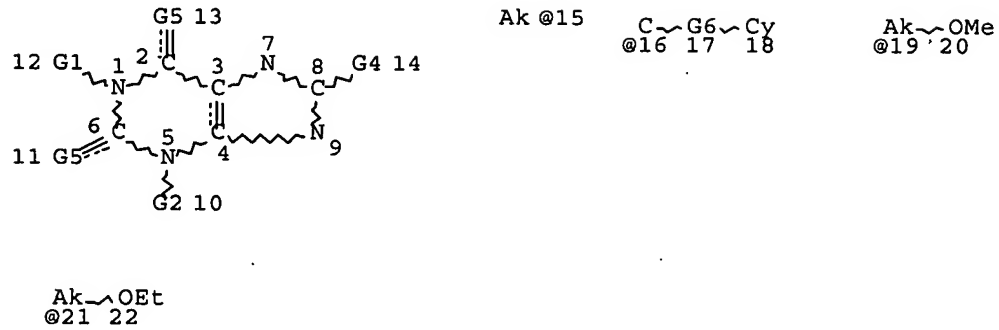


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'HOME' ENTERED AT 16:47:03 ON 12 APR 2007

SEARCH HISTORY

=> d stat que l27; d his nofile
L1 STR



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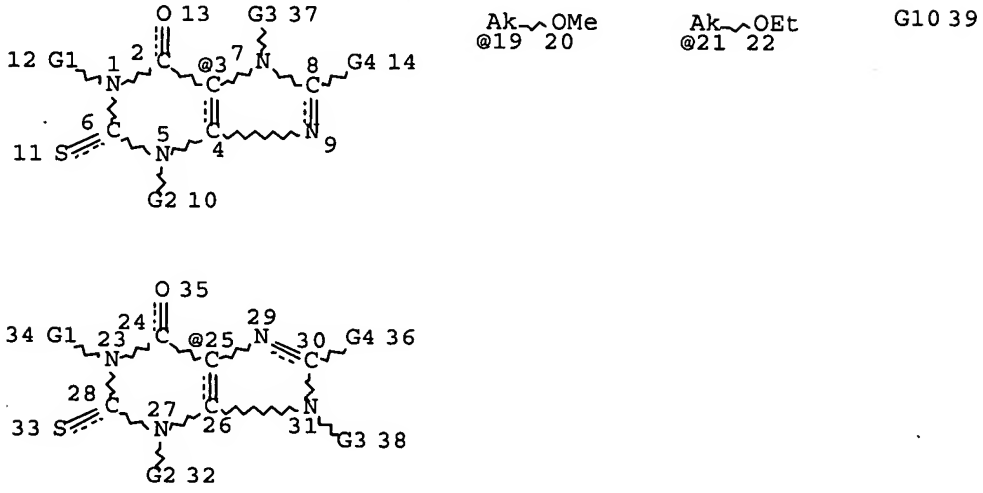
VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L4 17287 SEA FILE=REGISTRY SSS FUL L1
L24 STR



VAR G1=H/ME

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VAR G2=OME/OET/19/21
VAR G3=H/ME
VAR G4=H/ME
VAR G10=3/25
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CONNECT IS E2  RC AT  19
CONNECT IS E2  RC AT  21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  35

STEREO ATTRIBUTES: NONE
L27           2 SEA FILE=REGISTRY SUB=L4 SSS FUL L24

100.0% PROCESSED     229 ITERATIONS                                  2 ANSWERS
SEARCH TIME: 00.00.01



     (FILE 'HOME' ENTERED AT 16:04:30 ON 12 APR 2007)

     FILE 'REGISTRY' ENTERED AT 16:04:37 ON 12 APR 2007
L1              STR
L2             50 SEA SSS SAM L1
L3         115605 SEA SSS FUL L1 EXTEND
L4          17287 SEA SSS FUL L1
                  SAVE TEMP L4 BER537FULL/A
L5                STR L1
L6              1 SEA SUB=L4 SSS SAM L5
                  D SCAN
L7            229 SEA SUB=L4 SSS FUL L5 EXTEND
L8             17 SEA SUB=L4 SSS FUL L5
                  SAVE TEMP L8 BER537FULA/A

     FILE 'REGISTRY' ENTERED AT 16:17:11 ON 12 APR 2007
                  D STAT QUE L8

     FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007
L9              8 SEA ABB=ON  L8
                  D IBIB ED ABS HITSTR 1-8

     FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007
                  D STAT QUE L8
                  D COST

     FILE 'REGISTRY' ENTERED AT 16:18:23 ON 12 APR 2007
L10               STR L5
L11             1 SEA SUB=L4 SSS SAM L10
                  D SCAN
L12            52 SEA SUB=L4 SSS FUL L10 EXTEND
L13             6 SEA SUB=L4 SSS FUL L10
                  SAVE TEMP L13 BER537FULB/A

     FILE 'REGISTRY' ENTERED AT 16:27:53 ON 12 APR 2007
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                D STAT QUE L13

     FILE 'CAPLUS' ENTERED AT 16:27:53 ON 12 APR 2007
L14             4 SEA ABB=ON  L13
                D IBIB ED ABS HITSTR L14 1-4

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                D STAT QUE L13
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     FILE 'STNGUIDE' ENTERED AT 16:28:33 ON 12 APR 2007

     FILE 'REGISTRY' ENTERED AT 16:30:19 ON 12 APR 2007
L15             STR L5
L16             STR L10
L17           3 SEA SUB=L4 SSS SAM L16
                D SCAN
L18         263 SEA SUB=L4 SSS FUL L16 EXTEND
L19          23 SEA SUB=L4 SSS FUL L16
                SAVE TEMP L19 BER537FULC/A
L20             ANALYZE L19 1- LC :        7 TERMS
                D

     FILE 'REGISTRY' ENTERED AT 16:37:19 ON 12 APR 2007
                D STAT QUE L19

     FILE 'CAPLUS' ENTERED AT 16:37:19 ON 12 APR 2007
L21           18 SEA ABB=ON  L19

     FILE 'CAOLD' ENTERED AT 16:37:20 ON 12 APR 2007
L22             4 SEA ABB=ON  L19

     FILE 'CAPLUS, CAOLD' ENTERED AT 16:37:27 ON 12 APR 2007
L23           22 DUP REM L21 L22 (0 DUPLICATES REMOVED)
                     ANSWERS '1-18' FROM FILE CAPLUS
                     ANSWERS '19-22' FROM FILE CAOLD
                D IBIB ED ABS HITSTR 1-18
                D IALL HITSTR 19-22

     FILE 'HOME' ENTERED AT 16:38:01 ON 12 APR 2007
                D STAT QUE L19
                D SAVED

     FILE 'STNGUIDE' ENTERED AT 16:38:42 ON 12 APR 2007
                D COST

     FILE 'REGISTRY' ENTERED AT 16:39:32 ON 12 APR 2007
L24             STR L1\

     FILE 'STNGUIDE' ENTERED AT 16:42:39 ON 12 APR 2007
                D L24

     FILE 'REGISTRY' ENTERED AT 16:45:29 ON 12 APR 2007
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                D SCAN
L26           229 SEA SUB=L4 SSS FUL L24 EXTEND
L27             2 SEA SUB=L4 SSS FUL L24
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L28             1 SEA ABB=ON  L27
                D IBIB ED ABS HITSTR L28

     FILE 'HOME' ENTERED AT 16:47:03 ON 12 APR 2007
                D STAT QUE L27

=>
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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/13/07
Art Unit: 1624 Phone Number: 2- 0663 Serial Number: 10511537 C
Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): (PAPER) DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: ME

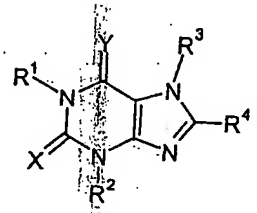
Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Date: _____ Search #6

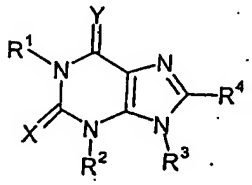
Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



(Ia)

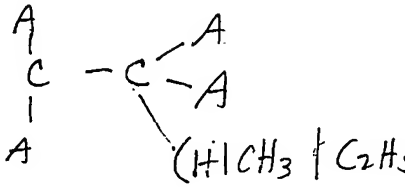
or



(Ib)

All A = H | CH_3

X = O Y = S

L = 
(H | CH_3 | C_2H_5 | C_3H_7)

R^4 = H | CH_3 | C_2H_5

R^3 = A

non i-

R^1 = H | CH_3 | ~~OOO~~ L

R^2 = L

20070412-10511537-dtr3

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Searcher: BOB
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: _____
Date Completed: 4-12-07
Searcher Prep & Review Time: 20
Online Time: 11

Type of Search

_____ NA Sequence (#)
_____ AA Sequence (#)
2 Structure (#)
_____ Bibliographic
_____ Litigation
_____ Fulltext
_____ Other

Vendors and cost where applicable

1166 STN _____ Dialog
_____ Questel/Orbit _____ Lexis/Nexis
_____ Westlaw _____ WWW/Internet

___In-house sequence systems

___Commercial ___Oligomer ___Score/Length
___ Interference ___ SPDI ___ Encode/Transl
_____ Other (specify)

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STRUCTURE FILE UPDATES:   11 APR 2007  HIGHEST RN 929721-97-1
DICTIONARY FILE UPDATES:  11 APR 2007  HIGHEST RN 929721-97-1

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1                STR
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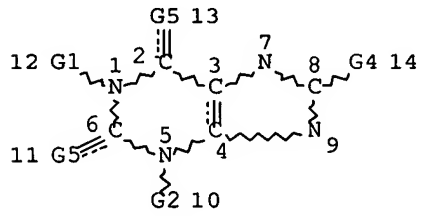

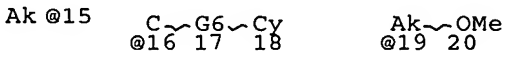

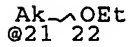


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VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  15
CONNECT IS E2  RC AT  19
CONNECT IS E2  RC AT  21
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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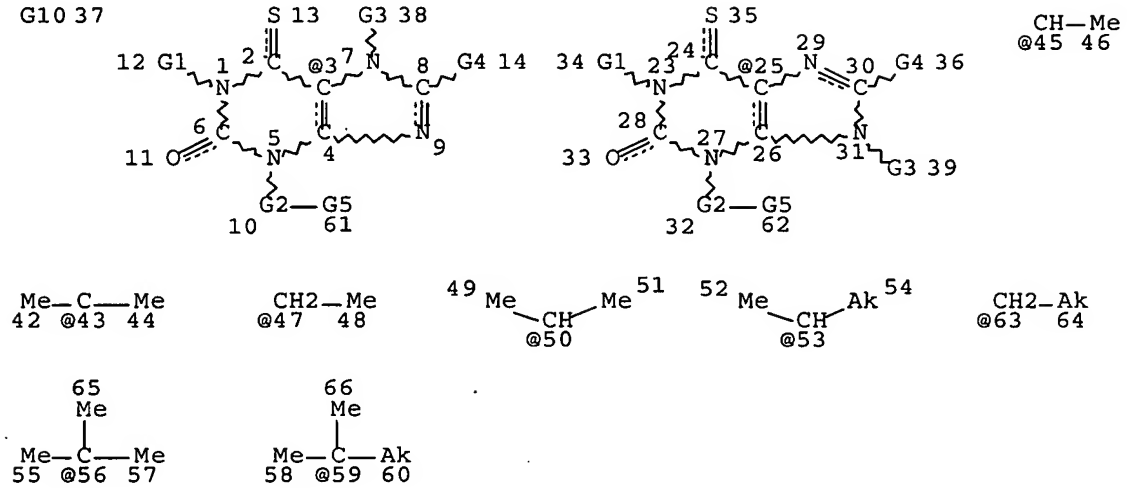

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VAR G3=H/ME
VAR G4=H/ME/ET
VAR G5=ME/47/63/50/53/56/59
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ECOUNT IS M2-X3 C AT 64

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 263 ITERATIONS 23 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 16:37:19 ON 12 APR 2007

FILE COVERS 1907 - 12 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

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L21 18 L19

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L22 4 L19

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DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
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PROCESSING COMPLETED FOR L21
PROCESSING COMPLETED FOR L22
L23           22 DUP REM L21 L22 (0 DUPLICATES REMOVED)
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                 ANSWERS '19-22' FROM FILE CAOLD

=> d ibib ed abs hitstr 1-18; d iall hitstr 19-22; fil hom

L23  ANSWER 1 OF 22  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:855927  CAPLUS  Full-text
DOCUMENT NUMBER:          139:350580
TITLE:                    Preparation of xanthinethione derivatives as
                          myeloperoxidase inhibitors
INVENTOR(S):              Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S):       Astrazeneca AB, Swed.
SOURCE:                   PCT Int. Appl., 55 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2003089430         A1    20031030    WO 2003-SE617            20030415
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     CA 2480452            A1    20031030    CA 2003-2480452          20030415
     AU 2003224548         A1    20031103    AU 2003-224548           20030415
     EP 1499613            A1    20050126    EP 2003-721211           20030415
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003009012         A     20050201    BR 2003-9012             20030415
     CN 1646531            A     20050727    CN 2003-808355           20030415
     JP 2005526836         T     20050908    JP 2003-586151           20030415
     NZ 535406             A     20060831    NZ 2003-535406           20030415
     ZA 2004007815         A     20051004    ZA 2004-7815             20040928
     US 2005234036         A1    20051020    US 2004-511537           20041015
     NO 2004004998         A     20050118    NO 2004-4998             20041117
PRIORITY APPLN. INFO.:                       SE 2002-1193         A   20020419
                                             SE 2002-2239         A   20020717
                                             WO 2003-SE617        W   20030415

OTHER SOURCE(S):          MARPAT 139:350580
ED   Entered STN:  31 Oct 2003
GI
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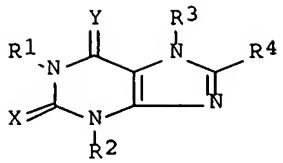

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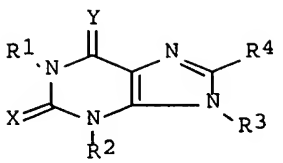


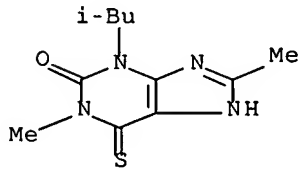
II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μM.

IT **618913-13-6P 618913-15-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

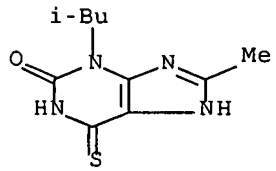
RN 618913-13-6 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1,8-dimethyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



RN 618913-15-8 CAPLUS

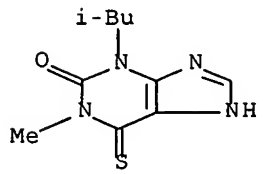
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-8-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:413184 CAPLUS Full-text
DOCUMENT NUMBER: 135:251414
TITLE: Structural predictions of adenosine 2B antagonist affinity using molecular field analysis

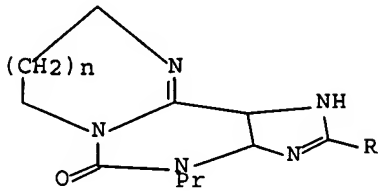
AUTHOR(S): Song, Yuqing; Coupar, Ian M.; Iskander, Magdy N.
CORPORATE SOURCE: Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia
SOURCE: Quantitative Structure-Activity Relationships (2001), 20(1), 23-30
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 Jun 2001
AB 3D structural evaluation of the adenosine 2B (A2B) antagonist binding site is the major aim for developing specific selective antagonists. In an attempt to deduce structural properties of the antagonist site, a pharmacophore model was developed using 85 known A2B antagonists. The mol. mechanics optimization methods were used to deduce the likely binding conformations of the antagonists at the binding site. Super-imposition of the antagonists was carried out using fit-atoms. This alignment was used to develop CoMFA models of the A2B antagonist binding site. The models possessed promising predictive ability as indicated by the high cross-validated correlation (q2 = 0.752, r2 = 0.982) and the prediction on the external test set. The analyses showed that steric and electrostatic interactions contributed to A2B antagonist biol. activity equally. The hydrogen-bond donor nature of the 7-position of xanthine (1 .apprx. 68) and 3-position of alloxazine (83) was essential for the biol. activity. In addition, the presence of more neg. charges on the 1-N position of xanthine and 10-N position of alloxazine increases biol. activity. The bulky aromatic substitutions on the 8-position of xanthine compds. improve activity, while an alkyl substitution on the 1-position of alloxazine might enhance activity. The model generated from this investigation produced important structural requirements, which will be used to optimize the structural complementarity of the antagonists at the A2B binding site.
IT **42458-91-3**, 1-Methyl-3-isobutyl-6-thioxanthine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural predictions of adenosine 2B antagonist affinity using mol. field anal.)
RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:77080 CAPLUS Full-text
DOCUMENT NUMBER: 120:77080
TITLE: Convenient synthesis of tricyclic purine derivatives
AUTHOR(S): Shimada, Junichi; Kuroda, Takeshi; Suzuki, Fumio

CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan
SOURCE: Journal of Heterocyclic Chemistry (1993), 30(1), 241-6
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:77080
ED Entered STN: 19 Feb 1994
GI



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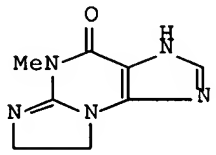
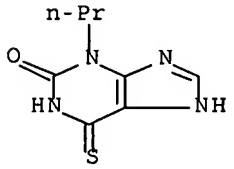


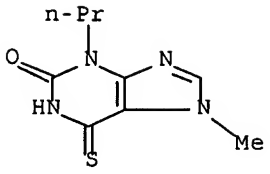
II

AB A convenient synthesis of the title compds. I (R = H, cyclopentyl; n = 0-2) and II is described. The syntheses of I and II were accomplished by treatment of 6-methylthio-7H-purin-2(3H)-ones or 2-benzylthio-1-methyl-9-triphenylmethyl-9H-purin-6(1H)-one (III) with the appropriate amino alc. followed by dehydrative cyclization using SOCl2. III was efficiently prepared by benzylation of 6-hydroxy-2-mercaptopurine followed by tritylation and N-methylation.

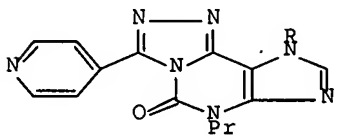
IT **105396-65-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)
RN 105396-65-4 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



IT **152036-07-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 152036-07-2 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-7-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:469819 CAPLUS Full-text
DOCUMENT NUMBER: 117:69819
TITLE: Facile synthesis of 9H-s-triazolo[3,4-i]purin-5(6H)-ones
AUTHOR(S): Shimada, Junichi; Suzuki, Fumio
CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan
SOURCE: Tetrahedron Letters (1992), 33(22), 3151-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:69819
ED Entered STN: 23 Aug 1992
GI



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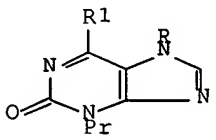
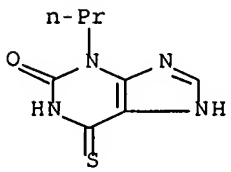


II

AB New tricyclic heterocycles, 9H-s-triazolo[3,4-i]purin-5(6H)-ones I (R = Me, H), were prepared from 6-methylthio-7H-purin-2(3H)-ones II (R = Me, PhCH2OCH2; R1 = MeS) via cyclization of II (R1 = isonicotinoylhydrazino).
IT **105396-65-4**, 3-Propyl-6-thioxanthine
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation or benzylation of)
RN 105396-65-4 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)

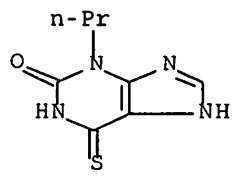


L23 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:536115 CAPLUS Full-text
DOCUMENT NUMBER: 115:136115
TITLE: Preparation of condensed purine derivatives as drugs
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Kuroda, Takeshi; Kubo, Kazuhiro; Karasawa, Akira; Ohno, Tetsuji; Ohmori, Kenji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 423805	A2	19910424	EP 1990-120056	19901019
EP 423805	A3	19920102		
EP 423805	B1	20000823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2028235	A1	19910421	CA 1990-2028235	19901019
CA 2028235	C	19970121		
JP 03204880	A	19910906	JP 1990-281578	19901019
US 5270316	A	19931214	US 1990-599758	19901019
AT 195739	T	20000915	AT 1990-120056	19901019
ES 2152207	T3	20010201	ES 1990-120056	19901019

PRIORITY APPLN. INFO.: JP 1989-273403 A 19891020
OTHER SOURCE(S): MARPAT 115:136115
ED Entered STN: 05 Oct 1991
GI For diagram(s), see printed CA Issue.
AB Title compds. I (A = Q, Q1, Q2; R1 = H, alkyl, alicyclic alkyl, noradamantan-3-yl, dicyclopropylmethyl, styryl; R2 = H, alkyl, alicyclic alkyl; R3 = H, alkyl, PhCH2; X1, X2 = H, alkyl, aralkyl, Ph; n = 0, 1) or a salt thereof, useful as diuretics, renal protecting agents, bronchodilators or hypotensives, are prepared Thus, H2NCH2CH2OH was added to 3,7-dihydro-7-methyl-6-(methylthio)-3-propyl-2H-purin-2-one (preparation given) and treated at 160° for 1 h to give the hydroxyethylamino derivative which was refluxed with POCl3 and after workup to give the imidazaopurinone II. II showed biol. activity as the above agents. Pharmaceutical formulations are given.
IT **105396-65-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)
RN 105396-65-4 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)

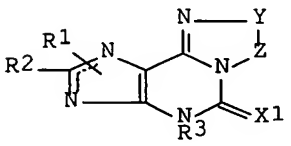


L23 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:491963 CAPLUS Full-text

DOCUMENT NUMBER: 115:91963
TITLE: Preparation and formulation of s-triazolo[3,4-i]purine derivatives as bronchodilators, diuretics, renal protectants, and antiamnestic agents
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ohmori, Kenji; Manabe, Haruhiko; Kubo, Kazuhiro; Karasawa, Akira; Ohno, Tetsuji; Shiozaki, Shizuo; Ishii, Akio; Shuto, Katsuichi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 417790	A2	19910320	EP 1990-117662	19900913
EP 417790	A3	19920318		
EP 417790	B1	19961204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 03204879	A	19910906	JP 1990-243248	19900913
JP 2980658	B2	19991122		
AT 145908	T	19961215	AT 1990-117662	19900913
ES 2097124	T3	19970401	ES 1990-117662	19900913
CA 2025413	A1	19910315	CA 1990-2025413	19900914
CA 2025413	C	19971104		
US 5173492	A	19921222	US 1991-752180	19910823
PRIORITY APPLN. INFO.:			JP 1989-239117 A	19890914
			JP 1989-261761 A	19891006
			US 1990-581562 B1	19900912

OTHER SOURCE(S): MARPAT 115:91963
ED Entered STN: 06 Sep 1991
GI



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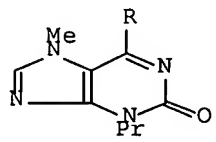

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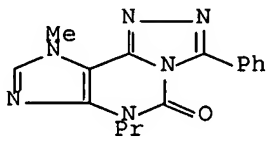


III

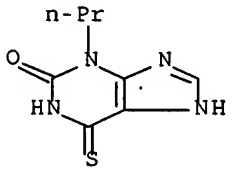
AB The title compds. [I; R1, R2 = H, alkyl, cycloalkyl, aralkyl, (substituted) aryl; R3 = alkyl, cycloalkyl, aralkyl, (substituted) aryl; X1 = O, S; YZ = N:CR4 or NR4C(:X2) wherein R4 = H, alkyl, (substituted) (hetero)aryl, X2 = O, S, NH] are prepared PhCONHNH2 was added to a suspension of II (R = MeS) (preparation given) in MePh, the mixture was refluxed to give 60% hydrazine

derivative II (R = PhCONHNH), which (2.64 g) was refluxed with 308 mg p-MeC6H4SO3H in MePh to give 67% title compound III. III showed IC50 of 4.1 μM in passive Schultz-Dale reaction (bronchodilatory effects) and diuretic activity at 25 mg/kg orally in rats. Also prepared and tested were 50 addnl. I. Tablet, syrup, powder, and capsule formulations were also given.

IT 105396-65-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of triazolopurine drugs)

RN 105396-65-4 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



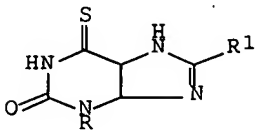
L23 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1986:626214 CAPLUS Full-text
DOCUMENT NUMBER: 105:226214
TITLE: 6-Thioxanthine derivatives
INVENTOR(S): Hofer, Peter
PATENT ASSIGNEE(S): Euro-Celtique S. A., Luxembourg
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 191313	A1	19860820	EP 1986-100544	19860117
EP 191313	B1	19921028		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4710503	A	19871201	US 1985-699254	19850207
IN 161914	A1	19880227	IN 1985-CA906	19851218
ZA 8509805	A	19860827	ZA 1985-9805	19851223
IL 77430	A	19881031	IL 1985-77430	19851224
AU 8651840	A	19860814	AU 1986-51840	19860103
AU 570142	B2	19880303		
AT 81858	T	19921115	AT 1986-100544	19860117
FI 8600285	A	19860808	FI 1986-285	19860121
FI 84180	B	19910715		
FI 84180	C	19911025		
DK 8600332	A	19860808	DK 1986-332	19860122
DK 161964	B	19910902		
DK 161964	C	19920210		
CN 86101050	A	19861112	CN 1986-101050	19860205
CN 1013676	B	19910828		
NO 8600424	A	19860808	NO 1986-424	19860206
NO 163569	B	19900312		

NO 163569	C	19900620			
CA 1275288	C	19901016	CA 1986-501288		19860206
JP 61183287	A	19860815	JP 1986-24248		19860207
JP 07080882	B	19950830			
US 4820709	A	19890411	US 1987-75937		19870722
US 4925847	A	19900515	US 1987-78545		19870728
US 5010081	A	19910423	US 1989-415970		19891002
JP 08099882	A	19960416	JP 1995-6756		19950119
JP 2888273	B2	19990510			
PRIORITY APPLN. INFO.:			US 1985-699254	A	19850207
			EP 1986-100544	A	19860117
			GB 1986-18931	A	19860802
			US 1987-78545	A1	19870728
			US 1989-322364	B2	19890313

OTHER SOURCE(S): CASREACT 105:226214
ED Entered STN: 26 Dec 1986
GI

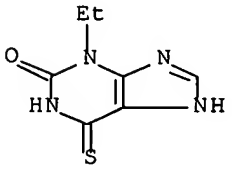


I

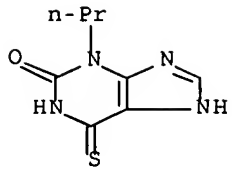
AB The title compds. I (R = Et, Pr, Bu; R1 = H, Me, Et) useful as bronchodilators (no data) were prepared Thus, 3-ethylxanthine in pyridine was treated with P2S5, H2O, NaOH, and acidified with 5N HCl to give I (R = Et; R1 = H).

IT **105396-64-3P 105396-65-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as bronchodilator)

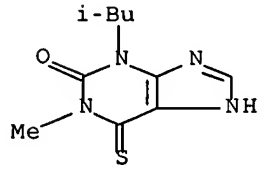
RN 105396-64-3 CAPLUS
CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-6-thioxo- (9CI) (CA INDEX NAME)



RN 105396-65-4 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)

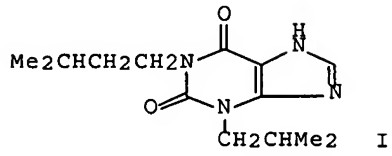


L23 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:435269 CAPLUS Full-text
DOCUMENT NUMBER: 95:35269
TITLE: Adenosine antagonism by purines, pteridines, and benzopteridines in human fibroblasts
AUTHOR(S): Bruns, Robert F.
CORPORATE SOURCE: Dep. Neurosci., Univ. California, La Jolla, CA, 92093, USA
SOURCE: Biochemical Pharmacology (1981), 30(4), 325-33
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB Testing of >100 purine bases and structurally related heterocycles as adenosine (I) [58-61-7] antagonists in VA13 fibroblasts (determined by cAMP increase) yielded 3 families of I antagonists: xanthines, benzo[g]pteridines, and 9-substituted adenines. For the xanthines, the optimal group at the 1-position was Bu (5-fold improvement vs. Me), at the 7-position was 2-chloroethyl (5-fold improvement vs. H), and at the 8-position was p-bromophenyl (100-fold improvement vs. H). The receptors apparently had butyl- and phenyl-sized pockets at the 1- and 8-positions, resp., since compds. with larger groups had greatly reduced activity.
IT **42458-91-3**
RL: BIOL (Biological study)
(adenosine receptor of fibroblast antagonism by)
RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:51769 CAPLUS Full-text
DOCUMENT NUMBER: 92:51769
TITLE: Effects of phosphodiesterase inhibitors on cyclic nucleotide levels and relaxation of pig coronary arteries
AUTHOR(S): Kramer, G. L.; Wells, J. N.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, 37232, USA

SOURCE: Molecular Pharmacology (1979), 16(3), 813-22
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



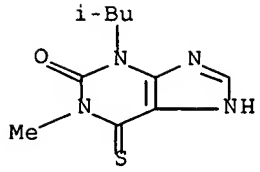
I

AB A series of xanthine derivs. and papaverine were studied to determine their abilities to alter tissue levels of cyclic AMP [60-92-4] and cyclic GMP [7665-99-8], inhibit cyclic nucleotide phosphodiesterase [50812-31-2] activities, and cause relaxation of pig coronary arteries. The agents exhibited a wide range of potencies to inhibit phosphodiesterase activities in the coronary artery supernatant fraction. In addition, some of these agents were up to 10 times more potent as inhibitors of cyclic GMP hydrolysis than of cyclic AMP hydrolysis, whereas others were 2-4 times more potent as inhibitors of cyclic AMP than of cyclic GMP hydrolysis. The rank order of potencies of these agents to cause relaxation of coronary artery strips was similar to the rank order of potencies to inhibit cyclic nucleotide phosphodiesterase activities. There were, however, some notable exceptions to the correlation between inhibition of cyclic nucleotide phosphodiesterase activities and relaxation. 1-Isoamyl-3-isobutylxanthine (I) [63908-26-9] was a more potent relaxing agent than might be expected from its relatively low potency to inhibit cyclic nucleotide hydrolysis in tissue exts. On the other hand, 1-methyl-3-isobutyl-7-(3-chlorobenzyl)-xanthine [58481-28-0] was 1 of the more potent inhibitors of cyclic nucleotide hydrolysis but was not as potent in causing relaxation as might have been expected. Exposure of the coronary artery strips to inhibitors caused increase in tissue levels of cyclic AMP and cyclic GMP and there was a statistically significant multiple linear regression of cyclic AMP and cyclic GMP levels on percent relaxation after 5 min of exposure to the agents. Cyclic AMP and cyclic GMP levels made approx. equal contributions to the regression of changes in percent relaxation, as determined by anal. of variance methods. While I did not fit the correlation between phosphodiesterase inhibition and potency to relax the arterial strips as well as the other agents, this agent caused unexpectedly large increases in cyclic AMP levels. Some agents caused relaxation accompanied by significant elevation of cyclic GMP levels and no significant change in cyclic AMP levels while other agents caused relaxation accompanied by significant increases in cyclic AMP but not cyclic GMP. These data offer some support for a hypothesis that both cyclic AMP and cyclic GMP are involved in the relaxation processes of pig coronary arteries.

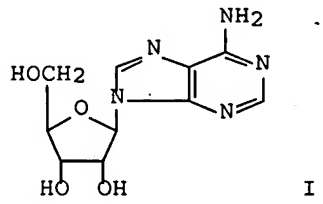
IT **42458-91-3**
RL: BIOL (Biological study)
(cyclic nucleotide of artery and artery contraction response to)

RN 42458-91-3 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:133356 CAPLUS Full-text
DOCUMENT NUMBER: 86:133356
TITLE: Effects of adenosine and related compounds on adenylate cyclase and cyclic AMP levels in smooth muscle
AUTHOR(S): McKenzie, Sheila G.; Frew, Robert; Bar, Hans P.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Alberta, Edmonton, AB, Can.
SOURCE: European Journal of Pharmacology (1977), 41(2), 193-203
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI

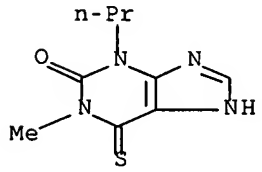


I

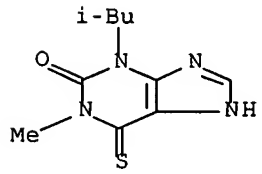
AB The hypotheses were tested that the relaxant effect of adenosine (I) [58-61-7] and related compds. in the longitudinal muscle of the rabbit small intestine involves interaction with adenylate cyclase [9012-42-4] and/or the elevation of tissue cyclic AMP [60-92-4] levels. Adenylate cyclase was prepared by gentle homogenization of an isolated smooth muscle cell fraction obtained after collagenase digestion of longitudinal muscle strips. A number of analogs and derivs. of I possessing a primary or secondary 6-amino group inhibited the enzyme similarly to I; however, there was no correlation between compds. known to relax the intact tissue and the existence, or the degree of, cyclase inhibition. Isolated muscle strips were exposed to adrenaline bitartrate [51-42-3], DL-isoprenaline-HCl [949-36-0], I, or ATP [56-65-5], at doses causing 30-60% relaxation, for 60 s prior to sampling and anal. of cAMP content. While small increments in cAMP levels were found after administering adrenaline or isoprenaline, no change was found with I in the absence or presence of aminophylline [317-34-0] or 1-methyl-3-isobutylxanthine [28822-58-4]. Neither adenylate cyclase inhibition nor changes in cAMP levels appear to be part of the mechanism of the smooth muscle relaxant action of I or ATP.

IT **42458-88-8 42458-91-3**
RL: BIOL (Biological study)
(adenylate cyclase of intestine smooth muscle response to)

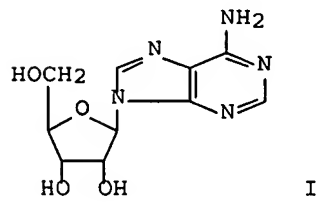
RN 42458-88-8 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:133355 CAPLUS Full-text
DOCUMENT NUMBER: 86:133355
TITLE: Characteristics of the relaxant response of adenosine and its analogs in intestinal smooth muscle
AUTHOR(S): McKenzie, Sheila G.; Frew, Robert; Bar, Hans P.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Alberta, Edmonton, AB, Can.
SOURCE: European Journal of Pharmacology (1977), 41(2), 183-92
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI

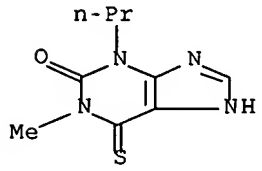


I

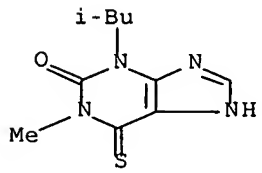
AB Several characteristics of the relaxant response of the isolated longitudinal muscle of the rabbit small intestine in response to the administration of adenosine (I) [58-61-7] and related compds. are studied. Following administration of I or ATP [56-65-5] the preparation responded with a rapid initial suspension of spontaneous contractile activity followed by a secondary sustained phase of inhibition of lower magnitude. Cumulative application of relaxant doses of I or ATP caused a lesser total response than that obtained by single application of the cumulative dose. Neither procaine, lidocaine or guanethidine antagonized the responses to I or ATP and the responsiveness of muscles obtained from reserpinized animals appeared unchanged. A number of I derivs. and analogs was tested for the ability to relax the muscle. Generally, compds. containing a primary or secondary 6-amino group acted as agonists with the exception of 8-bromoadenosine [2946-39-6]. Inactive nucleosides did not modify the responsiveness of the muscle to I. Responses to I and ATP were not appreciably modified by papaverine, imidazole, dipyridamole, 6-(p-nitrobenzylthio)-purine riboside. Antagonism was observed, however, with phentolamine [50-60-2] and aminophylline [317-34-0]. Aminophylline at 100 μM inhibited responses to I over a wide dose range; this antagonism was surmountable by high doses of I. 1-Methyl-3- isobutylxanthine [28822-58-4] did not antagonize I responses. A number of 1,3-alkyl-6-thioxanthines did not modify the I response at doses that did not show any direct action. The results support the concept of an extracellular receptor site of I and its analogs and the absence of an indirect mechanism of action via nerve stimulation.

IT **42458-88-8 42458-91-3**
RL: BIOL (Biological study)
(intestine smooth muscle relaxation by adenosine and its analogs response to)

RN 42458-88-8 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)

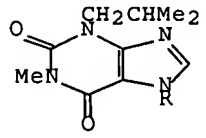


RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1976:130133 CAPLUS Full-text
DOCUMENT NUMBER: 84:130133
TITLE: Inhibition of separated forms of phosphodiesterases from pig coronary arteries by uracils and by 7-substituted derivatives of 1-methyl-3-isobutylxanthine
AUTHOR(S): Garst, J. E.; Kramer, G. L.; Wu, Y. J.; Wells, J. N.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, USA
SOURCE: Journal of Medicinal Chemistry (1976), 19(4), 499-503
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI

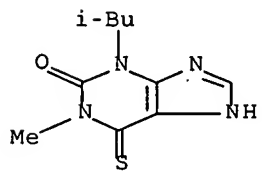


I

Rbs 8-14

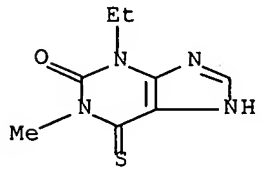
AB A series of 15 title xanthine derivs. (I; R = alkyl, aralkyl, alicyclicalkyl, propargyl, 4-picolyl), prepared by alkylation of 1-methyl-3-isobutylxanthine (I, R = H)(MIX) [28822-58-4] were tested for specificity of inhibition of chromatog.-separated cyclic nucleotide phosphodiesterase [50812-31-2] activity fractions I and II. I were generally much less potent than MIX as inhibitors of activity fraction II, but some retained the potency of MIX as inhibitors of activity fraction I. 1-Methyl-3-isobutyl-7-benzylxanthine (I, R = PhCH2) [58481-23-5] was 20-30 times more potent as an inhibitor of activity fraction I than of II, while retaining the potency of MIX against activity fraction I. A series of 1,3-dialkyluracils had low potency as phosphodiesterase inhibitors. Structure-activity relations were discussed.

IT **42458-91-3**
RL: BIOL (Biological study)
(cyclic nucleotide phosphodiesterases inhibition by)
RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)

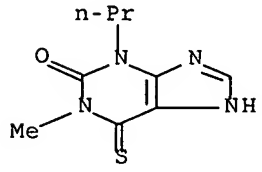


L23 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:427084 CAPLUS Full-text
DOCUMENT NUMBER: 79:27084
TITLE: Structure-activity relations. III. Bronchodilator

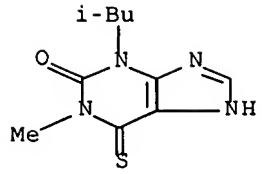
activity of substituted 6-thioxanthines
AUTHOR(S): Bowden, Keith; Wooldridge, Kenneth R. H.
CORPORATE SOURCE: Dep. Chem., Univ. Essex, Colchester/Essex, UK
SOURCE: Biochemical Pharmacology (1973), 22(9), 1015-21
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB A correlation of the bronchodilator activity of a series of substituted 6-thioxanthines (I) was made with partition parameters and (or) the steric effect of the 1- and 3-substituents. An increase in activity was observed on introduction of bulky substituents at R3 and particularly at R1. The 3-substituted series were also correlated by a Hansch relation involving partition factors alone. Thus, 1,3-dibutyl-6-thioxanthine [40915-18-2] was far more active than 1,3-dimethyl-6-thioxanthine [2398-70-1].
IT **42458-87-7 42458-88-8 42458-91-3**
42458-96-8
RL: BIOL (Biological study)
(bronchodilator)
RN 42458-87-7 CAPLUS
CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



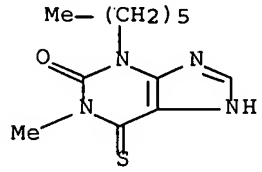
RN 42458-88-8 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



RN 42458-96-8 CAPLUS
CN 2H-Purin-2-one, 3-hexyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



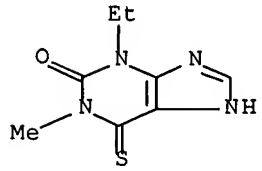
L23 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:429662 CAPLUS Full-text
DOCUMENT NUMBER: 57:29662
ORIGINAL REFERENCE NO.: 57:5924h-i,5925a-i,5926a-b
TITLE: The synthesis of some 6-thioxanthines
AUTHOR(S): Wooldridge, K. R. H.; Slack, R.
CORPORATE SOURCE: May Baker Ltd., Dagenham, UK
SOURCE: Journal of the Chemical Society (1962) 1863-28
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 57:29662
ED Entered STN: 22 Apr 2001
AB A series of 1,3- and 3,7-disubstituted 6-thioxanthines, of interest as broncho and coronary dilators, has been prepared by the selective thionation of the corresponding xanthines with P2S5 in C5H5N. 1,3,7-Trialkyl-6- thioxanthines could not be prepared in this way but were readily obtained front 1,3-dialkyl-6-thioxanthines. Theophylline (50 g.), 100 g. P2S3, and 1. dry C5H5N refluxed 8 hrs. with stirring, cooled, diluted with stirring during 1 hr. with 2 l. H2O, concentrated to about 1/3 volume, cooled, and filtered, and the residue dissolved in 2N NaOH, filtered, and repptd. with dilute HCl yielded 51 g. 1,3-dimethyl-6-thioxanthine (I), pale yellow needles, m. 323-5° (decomposition) (EtOH or H2O). 6-Thiotheobromine (75 g.) with 150 g. P2S5 gave similarly 72 g. 3,7-dimethyl-6-thioxanthine (II), m. 300-1°. (MeNH)2CS (79 g.) added in portions with stirring during 0.5 hr. to 65 g. NCCH2CO2H in 156 g. Ac2O and 200 cc. AcOH at 65°, kept 2 hrs. at 65% evaporated at 69-5° in vacuo, and the gummy residue stirred at 50° with 200 cc. H2O and adjusted to pH 10 with 50% aqueous NaOH gave 65 g. 6-amino-1,3-dimethyl 2-thiouracil (III), prisms, m. 286-8° (EtOH). The crude III suspended in 6000 cc. H2O containing 25.5 g. NaNO2 at 80-90 °, 50 cc. AcOH added during 15 min., and the mixture stirred 15 min. at 80-90° and cooled yielded crude 5-NO derivative (IV) of III, blue-green amorphous solid, m. 215-16° (decomposition). The IV added in 5-g. portions to 2.5 l. H2O at 70-80° together with sufficient Na2S2O4 to discharge the color of the IV, cooled, and filtered, the residual 5-NH2 derivative of

III, m. 230-4°, added immediately to 500 cc. 2N H_2SO_4, the resulting sulfate (57 g.) boiled 0.5 hr. with 500 cc. $HCONH_2$, diluted with 250 cc. H_2O, and cooled, and the yellow solid dissolved in 300 cc. hot 17% NH_4OH, filtered, and acidified to pH 4 with AcOH yielded 47 g. 1,3dimethyl-2-thioxanthine, m. 344-8°. Me_2SO_4 (25.2 g.) added dropwise in 15 min. with stirring at 40° to 35 g. I and 100 cc. 2N NaOH, kept 0.5 hr. at 40°, cooled, and filtered gave 15 g. 1,3,7-trimethyl-6-thioxanthine (V), pale yellow prisms, m. 246-7°. II (17.5 g.) and 42.5 g. Me_2SO_4 gave 1 g. V, m. 247-9°. II(10g.)in 125 cc. 0.5N NaOH stirred 2 hrs. at room temperature with 10.7 g. MeI yielded 6.7 g. 1,2,3,4tetrahydro-3,7-dimethyl- 1-methylthiopurine, needles, m. 300-3° (H_2O). The appropriate urea was converted by the method of Traube [Ber. 33, 3035(1900)] or of Speer and Raymond (CA 48, 1346h) or of Montgomery (CA 50, 13932b) to the corresponding 1,3-dialkylxanthines (1- and 3-alkyl group and m.p. given): Me, $MeO(CH_2)_3$, 166-8°; Me, furfuryl, 255-8°; Et, iso-Bu, 195-7°; Pr, iso-Bu, 189-92°; Bu, Me, 207-10°. Similarly were prepared 3-isobutylxanthine (VI), m. 299-301°, and the 7-Me derivative of VII, m. 239-41°. P_2S_5 (600 g.) and 482 g. 3-isobutyl-1-methylxanthine in 4.2 l. dry C_5H_5N, refluxed 9 hrs. with stirring, cooled to about 40°, diluted carefully with H_2O, concentrated to about 2.5 l., diluted with 3.5 l. H_2O, and filtered, and the residue dissolved in 2.5 l. warm N NaOH, filtered, and acidified with concentrated HCl to pH 4 pp.d. 426 g. 3-isobutyl-1-methyl-6-thioxanthine (VII), yellow prisms, m. 170-2° (EtOH). Similarly were prepared the following 1,3-disubstituted-6-thioxanthines (1- and 3-substituent, m.p., and % yield given): Me, Me (VIII), 3235°, 94; Me, Et, 235-7°, 79; Me, Pr, 164-7°, 63; Me, Bu, 156-8°, 73; Me, Am, 169-70°, 50; Me, C_6H_{13}, 167-74°, 78; Me, iso-Am, 156-60°, 50; Me, $MeO(CH_2)_3$, 150-2°, 50; Me, $CH_2{:}CHCH_2$, 152-6°, 81; Me, $CH{:}CMeCH_2$, 195-8°, 47; Me, $PhCH_2$, 213-15°, 84; Me, $Ph(CH_2)_2$, 198-9°, 63; Me, furfuryl, 184-6°, 15; Et, Me, 235-9°, 76; Et, Et, 2568°, 72; Et, Bu, 175-8°, 74; Et, iso-Bu, 180-3°, 39; Et, $CH_2{:}CHCH_2$, 210-12°, 49; Pr, Pr, 212-15°, 89; Bu, Me, 295-8°, 84; Bu, Bu, 183-6°, 72. Similarly were prepared the following 8-substituted VIII (substituent, m.p., and % yield given): Me, 294-5°, 75; Et, 218-19°, 76; SH, 240° (decomposition), 83. I (42 g.) and 8.6 g. NaOH in 150 cc. H_2O stirred 0.5 hr. at room temperature, cooled, and filtered, and the dried Na salt (44 g.) of I dissolved in 200 cc. $HCONMe_2$, treated with stirring during 15 min. at room temperature with 18.6 g. $AcCH_2Cl$, stirred 0.5 hr., diluted with 300 cc. iced H_2O, and filtered gave 21.3 g. 7-$AcCH_2$ derivative (IX) of I, yellow needles, m. 208-10°. IX (21 g.), 269 g. paraformaldehyde, 11.9 g. piperidine-HCl, 1.6 cc. $Et_2O.BF_3$, and 200 cc. dry dioxane stirred 7 hrs. at 100° and filtered gave 23.0 g. 1,3-dimethyl-7(2-oxo-4-piperidinobutyl)-6-thioxanthine-HCl, yellow-brown prisms, m. 197-200°. In the same manner as VII were prepared the following 1,3,7-trisubstituted-6-thioxanthines (1-, 3-, and 7-substituents and m.p. given): Me, Me, Et, 22830°; Me, Me, $Et_2N(CH_2)_2$, 52-4°; Me, iso-Bu, $Et_2N(CH_2)_2$ |isolated as the (-)-di(p-toluoyl) D-tartrate], 120° (decomposition); Me, iso-Bu, $AcCH_2$, 170-4°; Bu, Me, Me, 118-19°. in the same manner were prepared the following 3,7-dialkyl-6thioxanthines (3- and 7-substituents and m.p. given): Me, Me, 300-1°; Bu, Me, 200-3°; iso-Bu, Me, 228-30°. Also prepared was 3-methyl-6-thioxanthine, m. 269-74°. Choline chloride (3.4 g.) in 900 cc. hot iso-PrOH treated with stirring with 150 g. 85% KOH in 600 cc. absolute MeOH, cooled to 0°, filtered, treated with 500 g. VII, warmed a few min., and evaporated in vacuo, the residual sirup dissolved in 1 l. hot isoPrOH, treated with C, filtered, diluted with 1 l. dry Et_2O, and cooled, and the precipitated filtered off gave 548 g. choline salt of VII, pale yellow prisms, m. 145-9°; their mother liquor evaporated, and the sirupy residue dissolved in H_2O and acidified to pH 4 with HCl gave 8 g. VII. Similarly were prepared the choline salts of the following 1,3-disubstituted-6-thioxan-thines (1- and 3-substituents, m.p. and % yield given): Me, Me (X), 145-7°, 47; Me, Et, 157-9°, 72; Me, Pr, 145-50°, 72; Me, Bu, 133-5°, 88; Me, Am, 150-3°, 93; Me, C_6H_{13}, 55-7°, 94; Me, iso-Bu, 148.5-9.5°, 92; Me, iso-Am, 125-8°, 90; Me, $CH_2{:}CHCH_2$, 172-5°, 73; Me, $CH_2{:}CMeCH_2$,

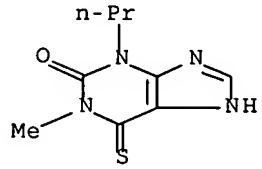
145-51°, 80; Me, PhCH2, 166-71°, 80; Me, Ph(CH2)2, 173-5°, 80; Et, Me, 157-8°, 70; Et, Et, 142-7°, 92; Et, Bu, 115-18°, 79; Pr, Pr, 114-18°, 57; Bu, Me, 105-9°, 62. Also prepared were 8-Me derivative of X, 175-6°, 65, and the 8-SH derivative of X, 209 11°, 70. The ultraviolet absorption maximum of a number of thioxanthines are tabulated.

IT **42458-87-7P**, Xanthine, 3-ethyl-1-methyl-6-thio-
42458-88-8P, Xanthine, 1-methyl-3-propyl-6-thio-
42458-91-3P, Xanthine, 3-isobutyl-1-methyl-6-thio-
42458-96-8P, Xanthine, 3-hexyl-1-methyl-6-thio-
93263-24-2P, Xanthine, 3-isobutyl-6-thio- **94733-95-6P**, Heteroxanthine, 3-isobutyl-6-thio- **96536-20-8P**, Choline, compound with 3-ethyl-1-methyl-6-thioxanthine **97212-72-1P**, Choline, compound with 1-methyl-3-propyl-6-thioxanthine **97406-00-3P**, Choline, compound with 3-isobutyl-1-methyl-6-thioxanthine **98174-21-1P**, Choline, compound with 3-hexyl-1-methyl-6-thioxanthine
RL: PREP (Preparation)
(preparation of)

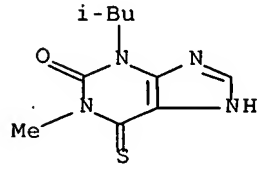
RN 42458-87-7 CAPLUS
CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



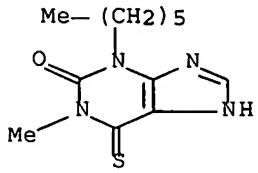
RN 42458-88-8 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



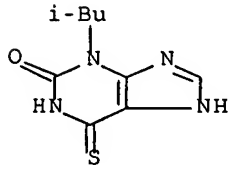
RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



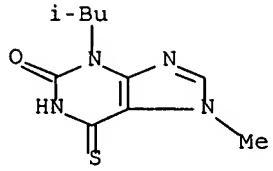
RN 42458-96-8 CAPLUS
CN 2H-Purin-2-one, 3-hexyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 93263-24-2 CAPLUS
CN Xanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



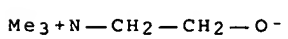
RN 94733-95-6 CAPLUS
CN Heteroxanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



RN 96536-20-8 CAPLUS
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

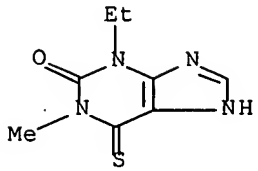
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

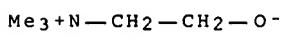
CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAPLUS
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

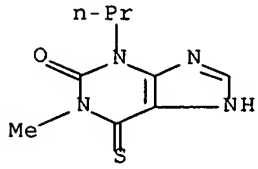
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

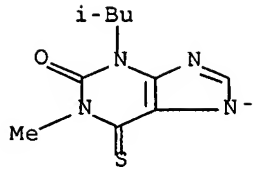
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAPLUS
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

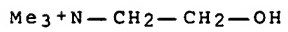
CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

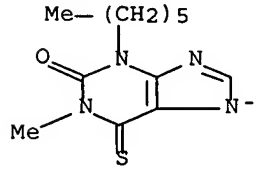
CRN 62-49-7
CMF C5 H14 N O



RN 98174-21-1 CAPLUS
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

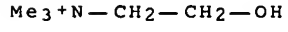
CM 1

CRN 98174-20-0
CMF C12 H17 N4 O S



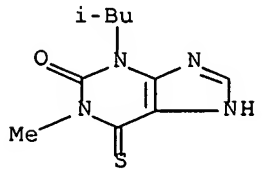
CM 2

CRN 62-49-7
CMF C5 H14 N O



L23 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:48836 CAPLUS Full-text
DOCUMENT NUMBER: 58:48836
ORIGINAL REFERENCE NO.: 58:8327a-b
TITLE: Observations concerning the effects of a thioxanthine upon the heart of the intact animal
AUTHOR(S): Maxwell, G. M.; Elliott, R. B.; Kneebone, G. M.

CORPORATE SOURCE: Univ. Adelaide
SOURCE: Australian J. Exp. Biol. Med. Sci. (1962), 40, 335-40
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB An intravenous dose of 1.0 mg. 3-isobutyl-1-methyl-6-thioxanthine/kg. administered to dogs gave statistically significant increases in respiratory rate, respiratory volume, O consumption, CO2 production, and pulse rate. Femoral and pulmonary arterial pressures decreased as did the calculated total peripheral resistance. Coronary blood flow and cardiac metabolic rates for O and CO2 increased. Cardiac efficiency and coronary vascular resistance decreased.
IT **42458-91-3**, Xanthine, 3-isobutyl-1-methyl-6-thio-
(heart response to)
RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo-
(9CI) (CA INDEX NAME)



L23 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:41798 CAPLUS Full-text
DOCUMENT NUMBER: 56:41798
ORIGINAL REFERENCE NO.: 56:7935c-f
TITLE: Structure-activity relations in a series of 6-thioxanthines with bronchodilator and coronary dilator properties
AUTHOR(S): Armitage, A. K.; Boswood, Janet; Large, B. J.
SOURCE: British Journal of Pharmacology and Chemotherapy (1961), 17, 196-207
CODEN: BJPCAL; ISSN: 0366-0826
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB The bronchodilator, coronary dilator, central stimulant, and diuretic activities of forty-seven 1,3-and 3,7-disubstituted and 1,3,7-trisubstituted 6-thioxanthines are reported. Bronchodilator activity was determined on the isolated guinea pig tracheal ring prepns. and coronary dilator activity on the dog heart-lung prepns. Diuretic activity was determined using conscious rats, and stimulant activity using mice. The in vivo bronchodilatory activity was determined by the protection afforded to guinea pigs against bronchoconstrictor aerosol. While choline 6-thiotheophyllinate is twice as active as choline theophyllinate as a broncho- and coronary dilator, several higher members of the theophylline series are more active than the 6-thio analogs. The 6-thiotheophylline is more active than the 6-thiotheobromine and 6-thiocaffeine. The 1,3-disubstituted compds. were more active as broncho- and coronary dilators than the 3,7-substituted compds. Maximum bronchodilator activity was achieved with relatively large alkyl groups in the 1 and 3 positions, and the 3-isobutyl derivative of 1-methyl-6-thiotheophylline was most active. Large groups in the 1-position may reduce oral absorption.

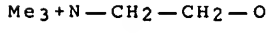
Compds. with unsatd. or substituted alkyl groups in the 3-position are less bronchoactive than compds. containing the corresponding saturated or unsubstituted groups. A 1-methyl group may be essential for coronary dilator activity. All the compds. tested had low diuretic activity. 6-Thiocaffeines, in contrast to caffeine, show no stimulant properties.

IT **96536-20-8**, Choline, compound with 3-ethyl-1-methyl-6-thioxanthine
97212-72-1, Choline, compound with 1-methyl-3-propyl-6-thioxanthine
97406-00-3, Choline, compound with 3-isobutyl-1-methyl-6-thioxanthine **98174-21-1**, Choline, compound with 3-hexyl-1-methyl-6-thioxanthine
(blood vessel and bronchial dilation by)

RN 96536-20-8 CAPLUS
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

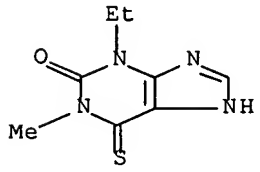
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

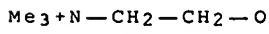
CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAPLUS
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

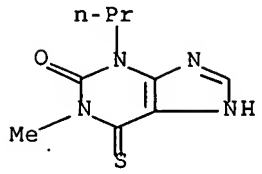
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

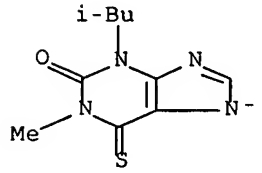
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAPLUS
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

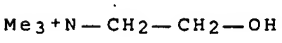
CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

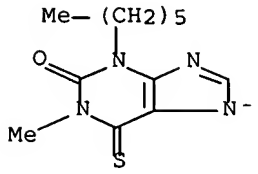
CRN 62-49-7
CMF C5 H14 N O



RN 98174-21-1 CAPLUS
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

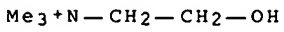
CM 1

CRN 98174-20-0
CMF C12 H17 N4 O S



CM 2

CRN 62-49-7
CMF C5 H14 N O



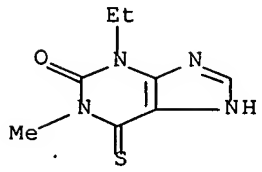
IT **96536-20-8**, Xanthine, 3-ethyl-1-methyl-6-thio-, compound with choline **97212-72-1**, Xanthine, 1-methyl-3-propyl-6-thio-, compound with choline **98174-21-1**, Xanthine, 3-hexyl-1-methyl-6-thio-, compound with choline
(blood-vessel and bronchial dilation by)
RN 96536-20-8 CAPLUS
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

CRN 44519-34-8
CMF C5 H13 N O

CM 2

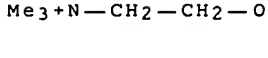
CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAPLUS
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

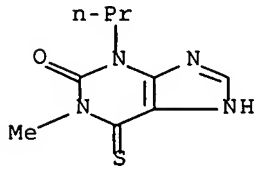
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

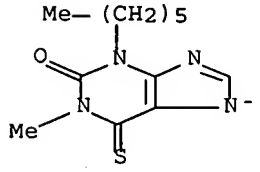
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 98174-21-1 CAPLUS
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

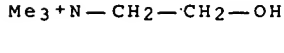
CM 1

CRN 98174-20-0
CMF C12 H17 N4 O S



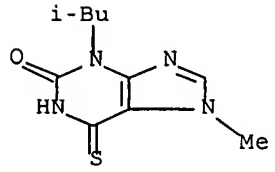
CM 2

CRN 62-49-7
CMF C5 H14 N O

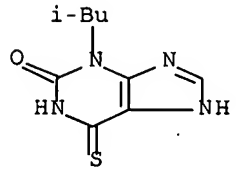


IT **94733-95-6**, Heteroxanthine, 3-isobutyl-6-thio-

(sodium derivative, blood vessel and bronchial dilation by)
RN 94733-95-6 CAPLUS
CN Heteroxanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



IT **93263-24-2**, Xanthine, 3-isobutyl-6-thio-
(sodium derivative, blood-vessel and bronchial dilation by)
RN 93263-24-2 CAPLUS
CN Xanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



ordered

L23 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1961:60865 CAPLUS Full-text
DOCUMENT NUMBER: 55:60865
ORIGINAL REFERENCE NO.: 55:11652a-d
TITLE: Thioxanthines with potent bronchodilator and coronary dilator properties
AUTHOR(S): Armitage, A. K.; Boswood, Janet; Large, B. J.
CORPORATE SOURCE: May and Baker, Dagenham, UK
SOURCE: British Journal of Pharmacology and Chemotherapy (1961), 16, 59-76
CODEN: BJPCAL; ISSN: 0366-0826
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB The pharmacol. properties of 2 new compds., choline 6-thiotheophyllinate (I) and the choline salt of 3-isobutyl-1-methyl-6-thioxanthine (M & B, 5924) (II) are described. As bronchodilators on the isolated guinea pig tracheal ring preparation, I and II were 57 and 5 times, resp., more active than choline theophyllinate (III). In protective effect against bronchioconstrictor aerosols, III (50 and 100 mg./kg., i.p.) was almost identical with that of I. II (100 mg./kg. orally) appeared to give more protection than III (200 mg./kg.). I and II had very little antihistaminic and antiacetylcholine activity. In cardiovascular studies on the anesthetized cats and dogs, all 3 compds. caused a transient fall in blood pressure. I and II were more potent than III as coronary dilators on the dog heart-lung preparation As diuretics they were less potent. In doses up to 20 mg./kg., III increased the voluntary locomotor activity of mice. A 50% increase was produced by 12 mg. of I and II each/kg. However, other doses from 5 to 80 mg./kg. either decreased motor

activity or had no effect. A 50% decrease in motor activity was produced by 32 mg. I/kg. and by 30 mg. II/kg. Toxic doses of III caused intense excitement and convulsions, whereas toxic doses of the thioxanthines caused sedation. Death in all cases was due to respiratory failure. In dogs, I in doses as high as 120 mg./kg., orally, caused no ill effects; II at 60 and 80 mg./kg. caused vomiting and retching lasting for about 1 h. II given i.v. to dogs in doses up to 3 mg./kg. caused vomiting, retching, excitation, and restlessness in contrast to the sedation seen in mice.

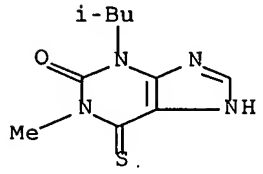
IT 857018-10-1, Xanthine, 3-isobutyl-1-methyl-6-thio-, compound with choline
(pharmacol. of)

RN 857018-10-1 CAPLUS

CN Xanthine, 3-isobutyl-1-methyl-6-thio-, compd. with choline (6CI) (CA INDEX NAME)

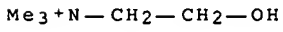
CM 1

CRN 42458-91-3
CMF C10 H14 N4 O S



CM 2

CRN 62-49-7
CMF C5 H14 N O



L23 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1961:56289 CAPLUS Full-text
DOCUMENT NUMBER: 55:56289
ORIGINAL REFERENCE NO.: 55:10804b-d
TITLE: 1,3-Dialkyl-6-thioxanthines: a new series of bronchodilators and coronary vasodilators
AUTHOR(S): Armitage, A. K.; Wooldridge, K. R. H.
CORPORATE SOURCE: May & Baker, Ltd., Dagenham, UK
SOURCE: Nature (London, United Kingdom) (1960), 188, 1107-8
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB Thioxanthines were prepared from the corresponding xanthines by refluxing for several hrs. with P2S5 in pyridine. Thionation occurred in the 6-position only. The choline salt of 3-isobutyl-1-methyl-6-thioxanthine (I), the most

active derivative in vitro for relaxation of the bronchial muscle and dilation of the coronary vessels, is pale-yellow, crystalline, solid, m. 145-7°, and >50% soluble in H2O at 20°. Choline 6-thiotheophyllinate (II), m. 146-9°, has similar solubility The thio derivs. are more active in vitro than in vivo. I is more active than II in dilating the coronary vessels of the dog heart-lung preparation or of the anesthetized dog, and in dilating the vessels of the hind leg of the dog perfused with heparinized blood.

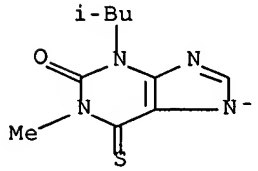
IT **97406-00-3**, Xanthine, 3-isobutyl-1-methyl-6-thio-, choline salt
(as bronchodilators and coronary vasodilators)

RN 97406-00-3 CAPLUS

CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

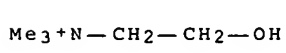
CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S

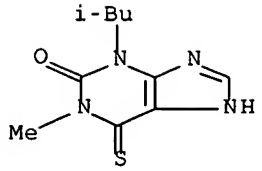


CM 2

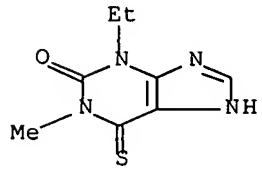
CRN 62-49-7
CMF C5 H14 N O



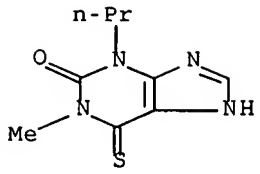
L23 ANSWER 19 OF 22 CAOLD COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: CA58:8327b CAOLD
TITLE: effects of simple liquids on the phagocytic properties of peritoneal macrophages - (I) stimulatory effects of glyceryl trioleate
AUTHOR NAME: Cooper, George N.; West, D.
INDEX TERM: **42458-91-3**
IT **42458-91-3**
RN 42458-91-3 CAOLD
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



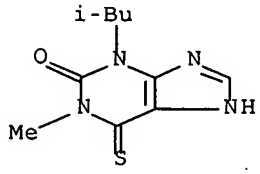
L23 ANSWER 20 OF 22 CAOLD COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: CA57:5924h CAOLD
TITLE: synthesis of some 6-thioxanthines
AUTHOR NAME: Wooldridge, Kenneth R. H.; Slack, R.
INDEX TERM: 2006-51-1 2398-70-1 3120-52-3 6501-95-7
6501-96-8 6603-63-0 13182-58-6 38759-03-4
38759-27-2 40915-18-2 **42458-87-7**
42458-88-8 42458-89-9 42458-90-2
42458-91-3 42458-92-4 42458-93-5 42458-94-6
42458-95-7 **42458-96-8** 42458-97-9 42458-98-0
42458-99-1 42459-00-7 42459-01-8 42459-02-9
42459-03-0 42459-04-1 42459-06-3 42459-07-4
42459-09-6 42459-10-9 63908-37-2 89620-34-8
90230-11-8 92985-74-5 **93263-24-2** 93967-36-3
94625-34-0 94733-92-3 94733-93-4 **94733-95-6**
94733-96-7 94763-87-8 96313-21-2 96535-23-8
96536-20-8 96536-21-9 96635-06-2 96652-89-0
96654-24-9 96986-49-1 **97212-72-1** 97282-72-9
97406-00-3 97406-02-5 97439-87-7 97556-86-0
97616-67-6 97767-38-9 97767-40-3 97769-20-5
97783-97-6 **98174-21-1** 98801-33-3 99688-81-0
106802-46-4
IT **42458-87-7** **42458-88-8** **42458-91-3**
42458-96-8 **93263-24-2** **94733-95-6**
96536-20-8 **97212-72-1** **97406-00-3**
98174-21-1
RN 42458-87-7 CAOLD
CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



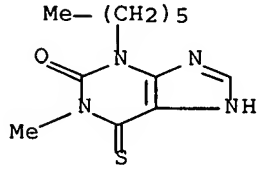
RN 42458-88-8 CAOLD
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



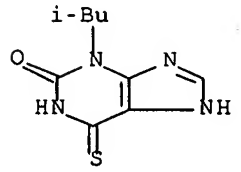
RN 42458-91-3 CAOLD
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



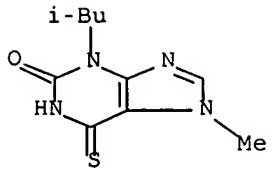
RN 42458-96-8 CAOLD
CN 2H-Purin-2-one, 3-hexyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 93263-24-2 CAOLD
CN Xanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



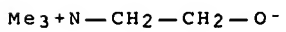
RN 94733-95-6 CAOLD
CN Heteroxanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



RN 96536-20-8 CAOLD
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

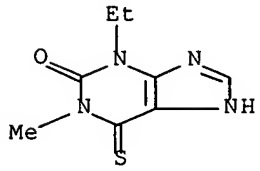
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

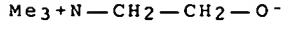
CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAOLD
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

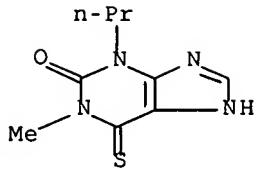
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

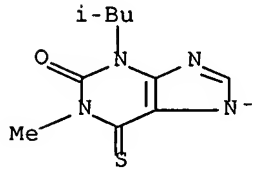
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAOLD
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

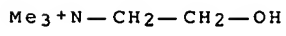
CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

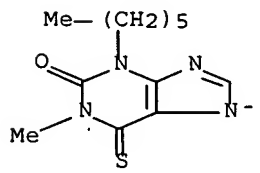
CRN 62-49-7
CMF C5 H14 N O



RN 98174-21-1 CAOLD
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

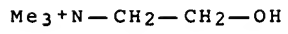
CM 1

CRN 98174-20-0
CMF C12 H17 N4 O S



CM 2

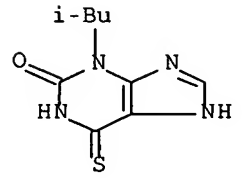
CRN 62-49-7
CMF C5 H14 N O



L23 ANSWER 21 OF 22 CAOLD COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: CA56:7935c CAOLD
TITLE: structure-activity relations in a series of 6-thioxanthines with bronchodilator and coronary dilator properties
AUTHOR NAME: Armitage, Alan K.; Boswood, J.; Large, B. J.
INDEX TERM:

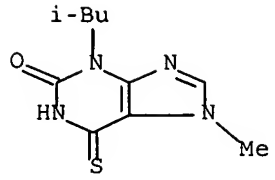
69-22-7	13182-58-6	56553-57-2	60725-48-6
77038-98-3	90117-29-6	90117-31-0	90230-11-8
92985-74-5	**93114-21-7**	93114-22-8	93262-67-0
93967-36-3	94031-71-7	94031-72-8	94072-68-1
94072-69-2	94733-92-3	95172-83-1	95172-89-7
95296-03-0	95324-23-5	95348-37-1	96313-22-3
96536-20-8	96536-21-9	96652-89-0	96955-54-3
96986-49-1	97194-78-0	97212-71-0	**97212-72-1**
97282-72-9	**97406-00-3**	97406-02-5	97439-87-7
97439-89-9	97616-67-6	97767-38-9	97767-40-3
97769-20-5	97783-97-6	**98174-21-1**	98801-33-3
99688-81-0	106802-46-4		

IT **93114-21-7** **94072-69-2** **96536-20-8**
97212-72-1 **97406-00-3** **98174-21-1**
RN 93114-21-7 CAOLD
CN Xanthine, 3-isobutyl-6-thio-, sodium deriv. (7CI) (CA INDEX NAME)



● Na

RN 94072-69-2 CAOLD
CN Heteroxanthine, 3-isobutyl-6-thio-, sodium deriv. (7CI) (CA INDEX NAME)



● Na

RN 96536-20-8 CAOLD
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

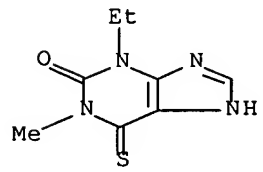
CM 1

CRN 44519-34-8
CMF C5 H13 N O

$Me_3{}^+N—CH_2—CH_2—O^-$

CM 2

CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAOLD
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

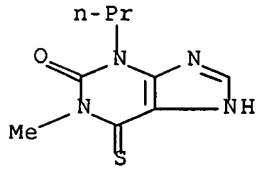
CM 1

CRN 44519-34-8
CMF C5 H13 N O

$Me_3{}^+N—CH_2—CH_2—O^-$

CM 2

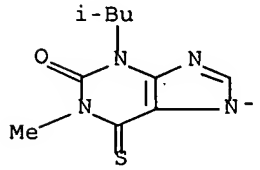
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAOLD
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



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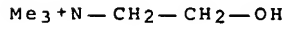
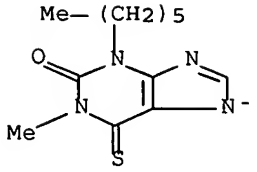
CRN 62-49-7
CMF C5 H14 N O



RN 98174-21-1 CAOLD
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

CRN 98174-20-0
CMF C12 H17 N4 O S



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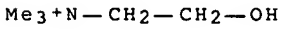
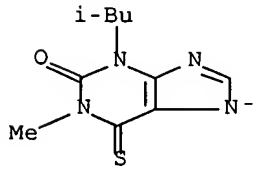


L23 ANSWER 22 OF 22 CAOLD COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: CA55:11652a CAOLD
TITLE: thioxanthines with potent bronchodilator and coronary dilator properties
AUTHOR NAME: Armitage, Alan K.; Boswood, J.; Large, B. J.
INDEX TERM: 90230-11-8 **97406-00-3**
IT **97406-00-3**
RN 97406-00-3 CAOLD
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

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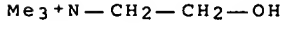
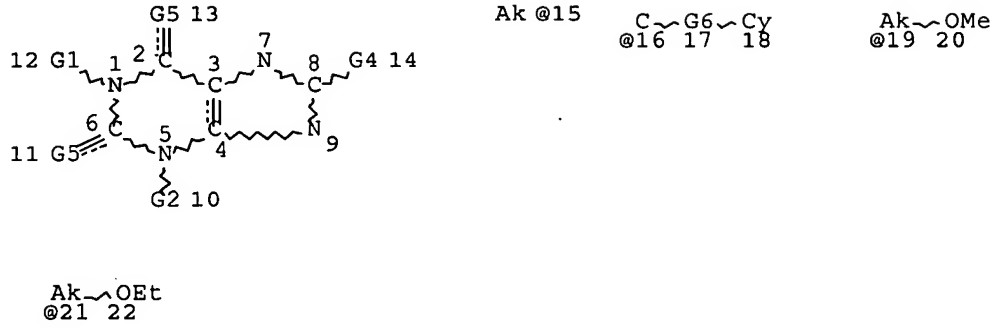


FILE 'HOME' ENTERED AT 16:38:01 ON 12 APR 2007

SEARCH HISTORY

=> d stat que l19; d his nofile
L1 STR



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VAR G2=16/15/OME/OET/19/21
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VAR G5=O/S
REP G6=(0-5) C
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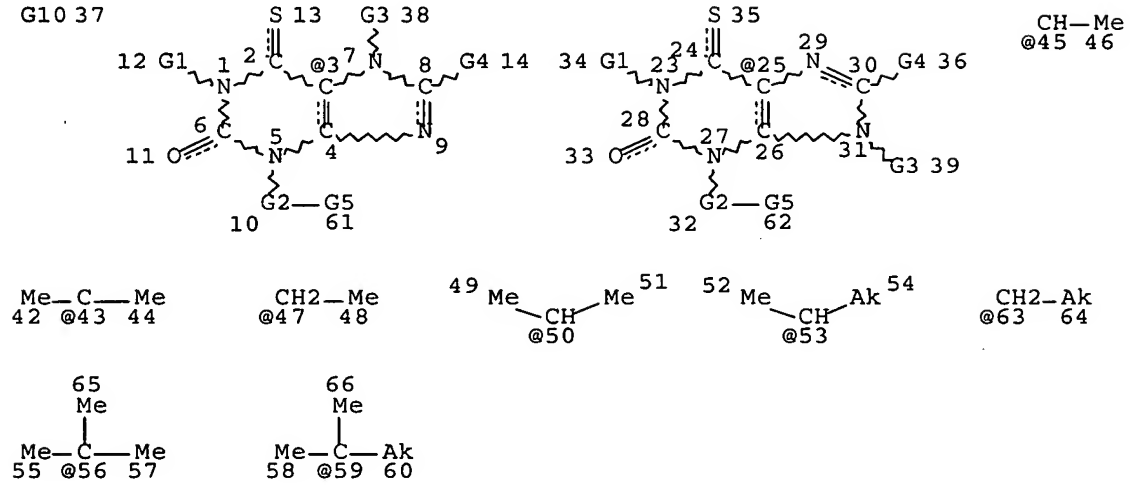
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L4 17287 SEA FILE=REGISTRY SSS FUL L1
L16 STR



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VAR G3=H/ME
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VAR G5=ME/47/63/50/53/56/59
VAR G10=3/25
NODE ATTRIBUTES:
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ECOUNT  IS M2-X3 C  AT  60
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  56

STEREO ATTRIBUTES: NONE
L19          23 SEA FILE=REGISTRY SUB=L4 SSS FUL L16

100.0% PROCESSED     263 ITERATIONS                          23 ANSWERS
SEARCH TIME: 00.00.01



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L2           50 SEA SSS SAM L1
L3       115605 SEA SSS FUL L1 EXTEND
L4        17287 SEA SSS FUL L1
               SAVE TEMP L4 BER537FULL/A
L5             STR L1
L6            1 SEA SUB=L4 SSS SAM L5
               D SCAN
L7          229 SEA SUB=L4 SSS FUL L5 EXTEND
L8           17 SEA SUB=L4 SSS FUL L5
               SAVE TEMP L8 BER537FULA/A

     FILE 'REGISTRY' ENTERED AT 16:17:11 ON 12 APR 2007
               D STAT QUE L8

     FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007
L9             8 SEA ABB=ON  L8
               D IBIB ED ABS HITSTR 1-8

     FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007
               D STAT QUE L8
               D COST

     FILE 'REGISTRY' ENTERED AT 16:18:23 ON 12 APR 2007
L10            STR L5
L11           1 SEA SUB=L4 SSS SAM L10
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                D SCAN
L12           52 SEA SUB=L4 SSS FUL L10 EXTEND
L13            6 SEA SUB=L4 SSS FUL L10
                SAVE TEMP L13 BER537FULB/A

     FILE 'REGISTRY' ENTERED AT 16:27:53 ON 12 APR 2007
                D STAT QUE L13

     FILE 'CAPLUS' ENTERED AT 16:27:53 ON 12 APR 2007
L14             4 SEA ABB=ON  L13
                D IBIB ED ABS HITSTR L14 1-4

     FILE 'HOME' ENTERED AT 16:28:06 ON 12 APR 2007
                D STAT QUE L13
                D COST

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     FILE 'REGISTRY' ENTERED AT 16:30:19 ON 12 APR 2007
L15             STR L5
L16             STR L10
L17             3 SEA SUB=L4 SSS SAM L16
                D SCAN
L18           263 SEA SUB=L4 SSS FUL L16 EXTEND
L19            23 SEA SUB=L4 SSS FUL L16
                SAVE TEMP L19 BER537FULC/A
L20             ANALYZE L19 1- LC :        7 TERMS
                D

     FILE 'REGISTRY' ENTERED AT 16:37:19 ON 12 APR 2007
                D STAT QUE L19

     FILE 'CAPLUS' ENTERED AT 16:37:19 ON 12 APR 2007
L21           18 SEA ABB=ON  L19

     FILE 'CAOLD' ENTERED AT 16:37:20 ON 12 APR 2007
L22            4 SEA ABB=ON  L19

     FILE 'CAPLUS, CAOLD' ENTERED AT 16:37:27 ON 12 APR 2007
L23           22 DUP REM L21 L22 (0 DUPLICATES REMOVED)
                     ANSWERS '1-18' FROM FILE CAPLUS
                     ANSWERS '19-22' FROM FILE CAOLD
                D IBIB ED ABS HITSTR 1-18
                D IALL HITSTR 19-22

     FILE 'HOME' ENTERED AT 16:38:01 ON 12 APR 2007
                D STAT QUE L19

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PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner # : 59193 Date: 4/13/07

Art Unit: 1624 Phone Number: 2- 0663 Serial Number: 10511537 B

Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: MG

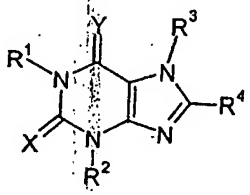
Inventors (please provide full names):

Earliest Priority Date: Seed #25

Search Topic:

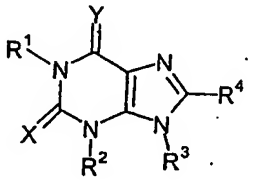
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



(Ia)

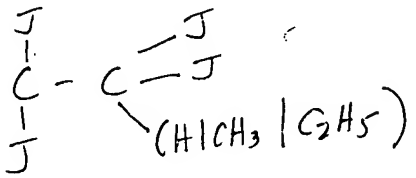
or



(Ib)

X = Y = S

all J, $R^1 = R^3 = R^4 = H \mid CH_3$

$R^2 =$ 

20070412-10511537-sfr-2

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STAFF USE ONLY

Searcher: Paul B

Searcher Phone #:

Searcher Location:

Date Searcher Picked Up:

Date Completed: 4-12-07

Searcher Prep & Review Time: 20

Online Time: 11

Type of Search

___ NA Sequence (#)

___ AA Sequence (#)

2 Structure (#)

___ Bibliographic

___ Litigation

___ Fulltext

___ Other

Vendors and cost where applicable

11 STN ___ Dialog

___ Questel/Orbit ___ Lexis/Nexis

___ Westlaw ___ WWW/Internet

___ In-house sequence systems

___ Commercial ___ Oligomer ___ Score/Length

___ Interference ___ SPDI ___ Encode/Transl

___ Other (specify)

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=> fil reg; d stat que l13; fil capl; s l13
FILE 'REGISTRY' ENTERED AT 16:27:53 ON 12 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   11 APR 2007  HIGHEST RN 929721-97-1
DICTIONARY FILE UPDATES:  11 APR 2007  HIGHEST RN 929721-97-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1                STR
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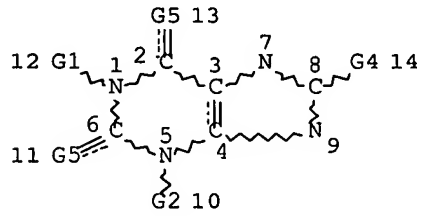

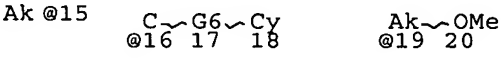

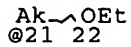


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VAR G1=H/15
VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  15
CONNECT IS E2  RC AT  19
CONNECT IS E2  RC AT  21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22
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STEREO ATTRIBUTES: NONE
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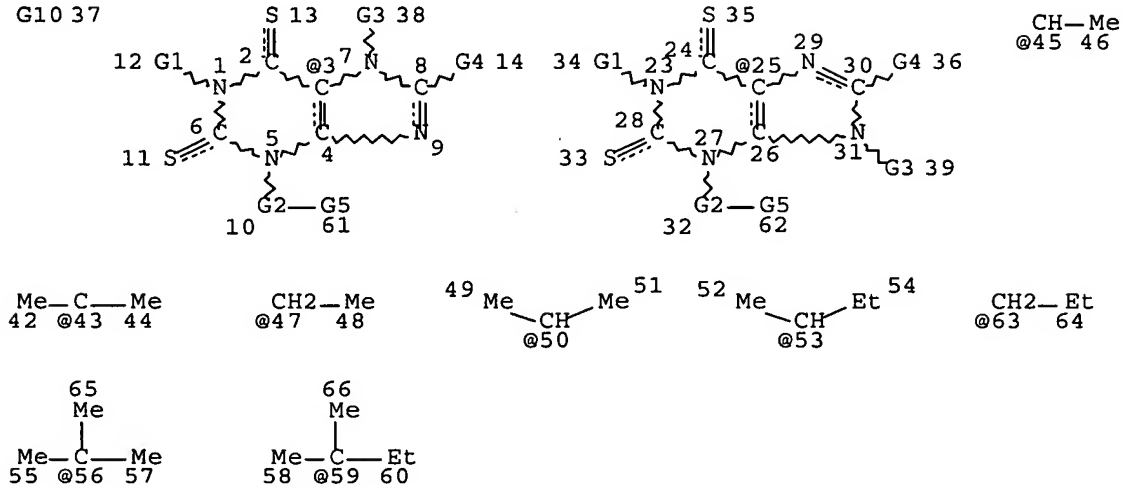

VAR G1=H/ME
VAR G2=CH2/45/43
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NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 52 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 16:27:53 ON 12 APR 2007

FILE COVERS 1907 - 12 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L14 4 L13

=> d ibib ed abs hitstr l14 1-4; fil hom

L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089430	A1	20031030	WO 2003-SE617	20030415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480452	A1	20031030	CA 2003-2480452	20030415
AU 2003224548	A1	20031103	AU 2003-224548	20030415
EP 1499613	A1	20050126	EP 2003-721211	20030415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009012	A	20050201	BR 2003-9012	20030415
CN 1646531	A	20050727	CN 2003-808355	20030415
JP 2005526836	T	20050908	JP 2003-586151	20030415
NZ 535406	A	20060831	NZ 2003-535406	20030415
ZA 2004007815	A	20051004	ZA 2004-7815	20040928
US 2005234036	A1	20051020	US 2004-511537	20041015
NO 2004004998	A	20050118	NO 2004-4998	20041117
PRIORITY APPLN. INFO.:			SE 2002-1193 A	20020419
			SE 2002-2239 A	20020717

WO 2003-SE617 W 20030415

OTHER SOURCE(S): MARPAT 139:350580
ED Entered STN: 31 Oct 2003
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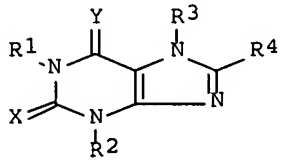

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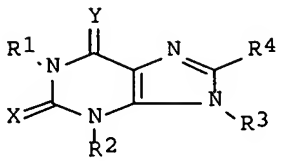


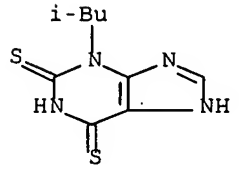
II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μM.

IT **618913-17-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-17-0 CAPLUS

CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:502824 CAPLUS Full-text
DOCUMENT NUMBER: 137:63122
TITLE: Preparation of purine derivatives or therapeutic use as phosphodiesterase IV inhibitors
INVENTOR(S): Chasin, Mark; Cavalla, David J.; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 285,473. CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6413975	B1	20020702	US 2000-539571	20000331
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
HU 200200938	A2	20021028	HU 2002-938	20000331
JP 2001316314	A	20011113	JP 2000-136383	20000509
US 2003073834	A1	20030417	US 2002-62280	20020201

PRIORITY APPLN. INFO.:

US 1999-285473	A2	19990402
IN 1994-CA514	A1	19940630
US 1997-963054	A2	19971103
US 1997-875487	A2	19971113
US 1998-151949	A2	19980911
US 1998-210556	A2	19981211
US 1998-210557	A2	19981211
US 1999-227057	A2	19990107
US 1999-237638	A2	19990126
US 1999-361196	A2	19990726
US 2000-506624	A2	20000218
US 2000-539571	A2	20000331
US 2000-547575	A2	20000412
US 2000-547898	A2	20000412
US 2000-636146	A2	20000810
US 2000-724321	B1	20001128

OTHER SOURCE(S): MARPAT 137:63122
ED Entered STN: 04 Jul 2002
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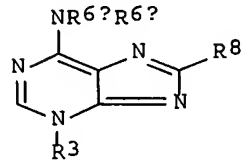

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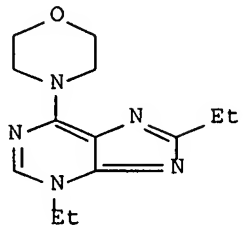


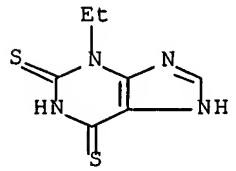
II

AB Purines, such as I [R3, R6a, R6b, R8 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase IV (PDE IV) inhibitors. Thus, 3,8-diethyl-6-morpholino- 3H-purine (II) was prepared by conversion of 3,8-diethyl-2-thioxanthine to 3,8-diethylhypoxanthine using 2N NaOH and nickel aluminum alloy, reaction of 3,8-diethylhypoxanthine to 3,8-diethyl-6-thiohypoxanthine using phosphorus pentasulfide in pyridine and, finally, reaction of 3,8-diethyl-6-thiohypoxanthine with morpholine. The prepared purine derivs. were assayed for PDE IV inhibition.

IT **162278-87-7P 162278-88-8P 162278-90-2P 439694-45-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of purine derivs. for therapeutic use as phosphodiesterase IV inhibitors)

RN 162278-87-7 CAPLUS
CN 1H-Purine-2,6-dithione, 3-ethyl-3,7-dihydro- (9CI) (CA INDEX NAME)



RN 162278-88-8 CAPLUS
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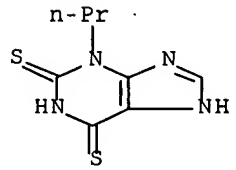

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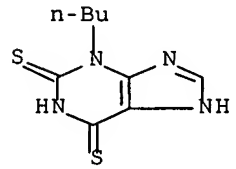

RN 439694-45-8 CAPLUS
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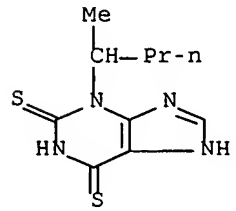

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:725418 CAPLUS Full-text
DOCUMENT NUMBER: 133:296324
TITLE: Synthesis and phosphodiesterase IV inhibition activity of purine derivatives
INVENTOR(S): Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig, Andre; Wintergest, Peter
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059449	A2	20001012	WO 2000-US8525	20000331
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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IN 181538	A1	19980711	IN 1995-CA1506	19951123
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EP 1169321	A2	20020109	EP 2000-919929	20000331
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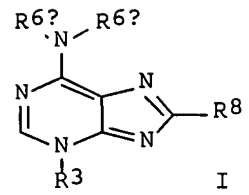
JP 2002541078	T	20021203	JP 2000-609014	20000331
BR 2000011182	A	20030610	BR 2000-11182	20000331
JP 2001316314	A	20011113	JP 2000-136383	20000509
PRIORITY APPLN. INFO.:			US 1999-285473 A	19990402
			IN 1994-CA514 A1	19940630
			WO 2000-US8525 W	20000331

OTHER SOURCE(S): MARPAT 133:296324
ED Entered STN: 13 Oct 2000
GI



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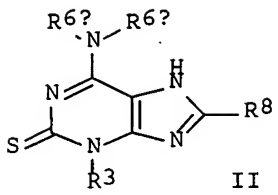

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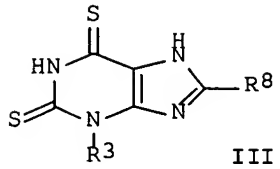

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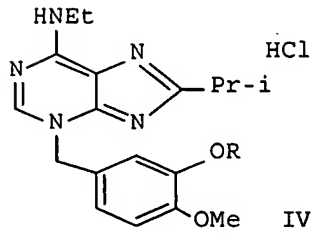

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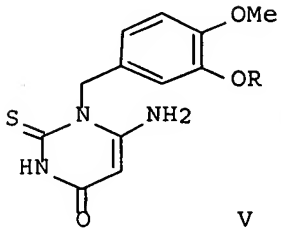

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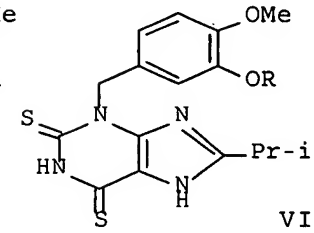


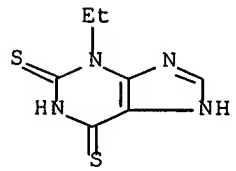
VI

AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH2)5) was prepared by etherification of isovanilline with cyclopentanol, oximation, reduction to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC50 of IV against phosphodiesterase IV inhibition was 0.32 μM. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

IT **162278-87-7P 162278-88-8P 162278-90-2P**
300783-45-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of purine derivs. as phosphodiesterase IV inhibitors)

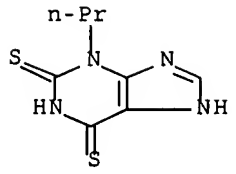
RN 162278-87-7 CAPLUS

CN 1H-Purine-2,6-dithione, 3-ethyl-3,7-dihydro- (9CI) (CA INDEX NAME)



RN 162278-88-8 CAPLUS

CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)



RN 162278-90-2 CAPLUS
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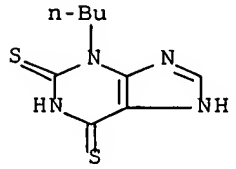

RN 300783-45-3 CAPLUS
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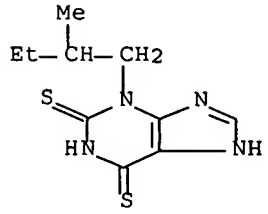

L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:492020 CAPLUS Full-text
DOCUMENT NUMBER: 122:239459
TITLE: Preparation of purines, isoguanines, and dithioxanthines as phosphodiesterase-IV inhibitors
INVENTOR(S): Cavalla, David; Hofer, Peter; Gehrig, Anddre; Wintergest, Peter
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500516	A1	19950105	WO 1994-GB1334	19940621
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    CA 2165433          A1    19941223    CA 1994-2165433        19940621
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    AU 9469771          A     19950117    AU 1994-69771          19940621
    AU 683270           B2    19971106
    EP 705265           A1    19960410    EP 1994-918456         19940621
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    CN 1045778          B     19991020
    HU 74176            A2    19961128    HU 1995-3545           19940621
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    JP 3350550          B2    20021125
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    US 5939422          A     19990817    US 1996-578580         19960408
    US 6310205          B1    20011030    US 1999-237638         19990126
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PRIORITY APPLN. INFO.:                      GB 1993-12853       A  19930622
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OTHER SOURCE(S):          MARPAT 122:239459
ED   Entered STN:  18 Apr 1995
GI
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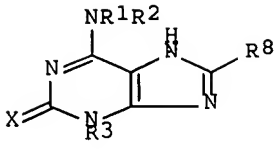

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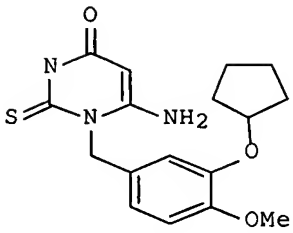
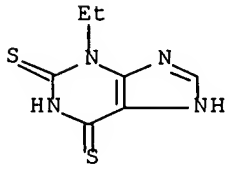


II

AB Title compds. [e.g., I; R1-R3,R8 = H, (cyclo)alkyl, (hetero)aryl, etc.; NR1R2 = heterocyclyl] were prepared Title compds. have bronchial and tracheal relaxation and/or antiinflammatory activity. Thus, isovanillin was converted in 5 steps to 3,4-(HO)(MeO)C6H3CH2NHCSNH2 which was cyclocondensed with NCCH2CO2Et to give thiouracil II. The latter was converted in 3 steps to 6-amino-1-(3-cyclopentyloxy-4-methoxybenzyl)-5- isobutyrylamino-2-thiouracil which was cyclized and the product converted in 4 steps to I.HCl (R1 = Et, R2 = H, R3 = 3-cyclopentyloxy-4- methoxybenzyl, R8 = CHMe2)(III). III gave 64% inhibition of ovalbumin-induced bronchoalveolar eosinophil production in guinea pigs at 5mg/kg i.p.

IT **162278-87-7P 162278-88-8P 162278-90-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of purines, isoguanines, and dithioxanthines as phosphodiesterase-IV inhibitors)

RN 162278-87-7 CAPLUS
CN 1H-Purine-2,6-dithione, 3-ethyl-3,7-dihydro- (9CI) (CA INDEX NAME)



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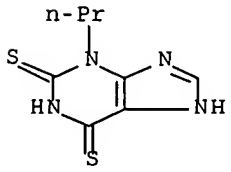

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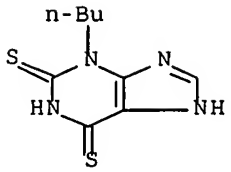

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SEARCH HISTORY

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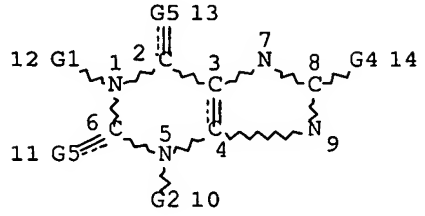

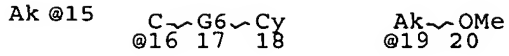

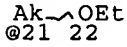

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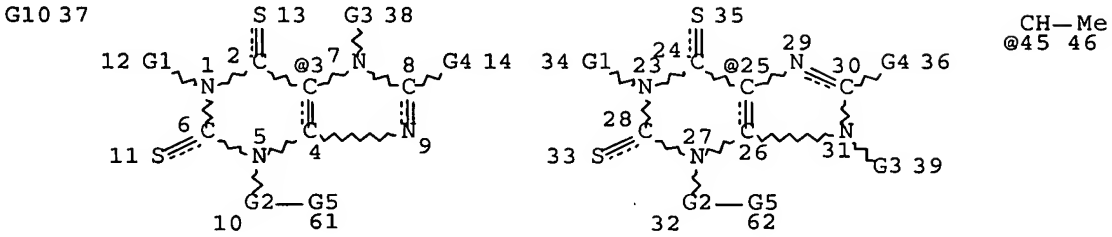

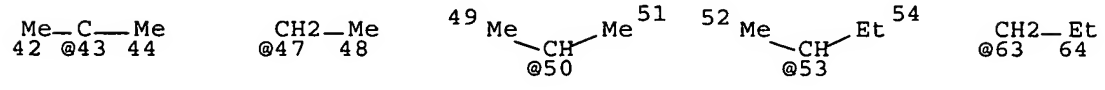

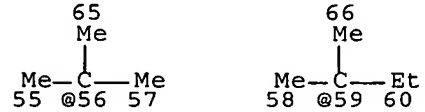

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NUMBER OF NODES IS  56

STEREO ATTRIBUTES: NONE
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Author Search

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FILE COVERS 1907 - 13 Apr 2007  VOL 146 ISS 17
FILE LAST UPDATED: 12 Apr 2007  (20070412/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE
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Search 3

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=> D QUE L8
L5           378 SEA FILE=CAPLUS ABB=ON  PLU=ON  HANSON S?/AU
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L7            17 SEA FILE=CAPLUS ABB=ON  PLU=ON  TIDEN A?/AU
L8             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L5 OR L6) AND L7


=> D IBIB ED ABS L8 1

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:855927  CAPLUS  Full-text
DOCUMENT NUMBER:          139:350580
TITLE:                    Preparation of xanthinethione derivatives as
                          myeloperoxidase inhibitors
INVENTOR(S):              Hanson, Sverker; Nordvall, Gunnar;
                          Tiden, Anna-Karin
PATENT ASSIGNEE(S):       Astrazeneca AB, Swed.
SOURCE:                   PCT Int. Appl., 55 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2003089430         A1    20031030    WO 2003-SE617            20030415
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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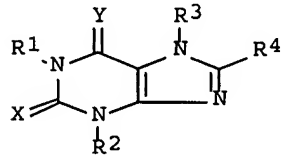
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2480452	A1	20031030	CA 2003-2480452	20030415
AU 2003224548	A1	20031103	AU 2003-224548	20030415
EP 1499613	A1	20050126	EP 2003-721211	20030415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009012	A	20050201	BR 2003-9012	20030415
CN 1646531	A	20050727	CN 2003-808355	20030415
JP 2005526836	T	20050908	JP 2003-586151	20030415
NZ 535406	A	20060831	NZ 2003-535406	20030415
ZA 2004007815	A	20051004	ZA 2004-7815	20040928
US 2005234036	A1	20051020	US 2004-511537	20041015
NO 2004004998	A	20050118	NO 2004-4998	20041117
PRIORITY APPLN. INFO.:			SE 2002-1193 A	20020419
			SE 2002-2239 A	20020717
			WO 2003-SE617 W	20030415

OTHER SOURCE(S): MARPAT 139:350580
ED Entered STN: 31 Oct 2003
GI



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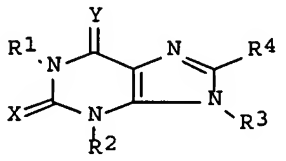

II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μM.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Structure Search

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L1              STR

Structure attributes must be viewed using STN Express query preparation:
Uploading L11.str
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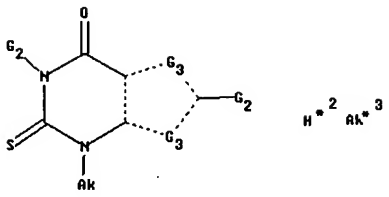

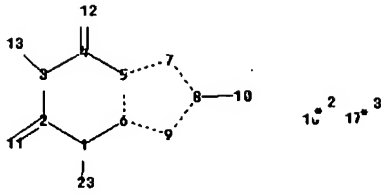

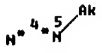

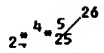

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10  11  12  13  16  17  23  24  25  26
ring nodes :
1  2  3  4  5  6  7  8  9
chain bonds :
1-23  2-11  3-13  4-12  8-10  25-26
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-9  7-8  8-9
exact/norm bonds :
1-2  1-6  1-23  2-3  2-11  3-4  3-13  4-5  4-12  5-6  5-7  6-9  7-8  8-9  8-10  25-
26


G1

G2:[*1],[*2]

G3:[*3],[*4]

Connectivity :
11:1 E exact RC ring/chain  17:1 E exact RC ring/chain  23:1 E exact RC ring/chain
24:2 E exact RC ring/chain  26:1 E exact RC ring/chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:CLASS
11:CLASS  12:CLASS  13:CLASS  16:CLASS  17:CLASS  23:CLASS  24:CLASS  25:CLASS
26:CLASS
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Saturation              : Saturated
23:
Saturation              : Saturated
26:
Saturation              : Saturated

Element Count :
Node 17: Limited
    C,C1-3

Node 26: Limited
    C,C1-3



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L4          48 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3


=> S L4 NOT L8
L9          47 L4 NOT L8

=> D IBIB ED ABS HITSTR 1-47

L9   ANSWER 1 OF 47  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2004:205972  CAPLUS  Full-text
DOCUMENT NUMBER:         142:176578
TITLE:                   Product class 17: purines
AUTHOR(S):               Seela, F.; Ramzaeva, N.; Rosemeyer, H.
CORPORATE SOURCE:        Germany
SOURCE:                  Science of Synthesis (2004), 16, 945-1108
                         CODEN: SSCYJ9
PUBLISHER:               Georg Thieme Verlag
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
ED   Entered STN:  15 Mar 2004
AB   A review.  Methods for preparing purines are reviewed including cyclization,
     ring transformation, and substituent modification.  Oxidation of purines is
     included.
IT   28139-02-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and oxidation of purines via cyclization, ring transformation
and
        substituent modification)
RN   28139-02-8  CAPLUS
CN   6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI)  (CA INDEX
     NAME)
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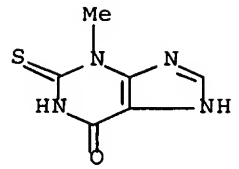
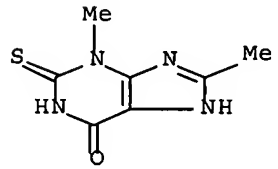


IT **91725-06-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and oxidation of purines via cyclization, ring transformation and
substituent modification)
RN 91725-06-3 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 762 THERE ARE 762 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:706960 CAPLUS Full-text
DOCUMENT NUMBER: 139:230796
TITLE: Synthesis of new purine derivatives
INVENTOR(S): Miyamoto, Kenichi; Sawanishi, Hiroyuki; Suzuki, Koichi; Yamamoto, Manabu; Shimura, Susumu
PATENT ASSIGNEE(S): Lotte Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003252875	A	20030910	JP 2002-58098	20020304
KR 2003072251	A	20030913	KR 2003-13401	20030304

PRIORITY APPLN. INFO.: JP 2002-58098 A 20020304
OTHER SOURCE(S): MARPAT 139:230796
ED Entered STN: 10 Sep 2003
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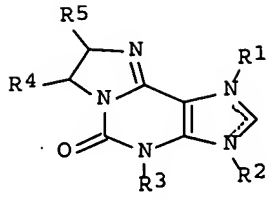

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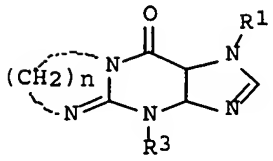


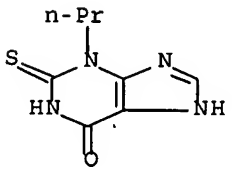
II

AB The patent relates to the preparation of purine derivs. and salts for pharmaceutical uses such as PDE IV isoenzyme inhibitor. The purine derivs. have the following formula (I) wherein R1, R2, R3 are hydrogen, or hydroxy, low alkyloxy, acyl substituted C1-C6 alkyl, or phenyl; and R4, and R5 are independently hydroxy, low alkyloxy, acyl substituted C1-C6 alkyl, or Ph group; and pharmaceutically compatible salts. The purine derivs. and pharmaceutically compatible salts may have the following formula (II) wherein R1, R2 are hydrogen, or hydroxy, low alkyloxy, acyl substituted C1-C6 alkyl, or phenyl; and n = 2 or 3. Thus, 8-methyl-4-propyl-4,5,7,8-tetrahydro-1H-imidazole-[2,1,i]purine-5-one prepared from 6-[(2-hydroxy-1-methyl)ethyl]amino-3-propylpurine-2-one in presence of triethylamine, and methanesulfonyl chloride was evaluated for PDE I test and gave greater activity than the control using Denoufylline.

IT **156733-29-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation of new purine derivs.)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:723414 CAPLUS Full-text

DOCUMENT NUMBER: 138:137075

TITLE: Synthesis and cyclic AMP phosphodiesterase 4 isoenzyme inhibitory activity of heterocycle condensed purines

AUTHOR(S): Suzuki, Hirokazu; Yamamoto, Manabu; Shimura, Susumu; Miyamoto, Ken-ichi; Yamamoto, Kenji; Sawanishi, Hiroyuki

CORPORATE SOURCE: Department of Synthetic Chemistry, Hokuriku University, Kanazawa, 920-1181, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (2002), 50(9), 1163-1168
CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:137075
ED Entered STN: 24 Sep 2002
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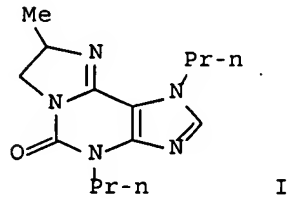
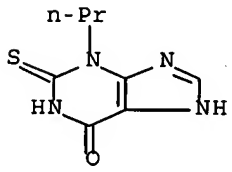


I

AB To reverse the adverse reactions of alkylxanthines and to develop novel inhibitors of cAMP phosphodiesterase 4 (PDE4), a series of heterocycle [a]-, [b]-, [c,d]-, and [i]-condensed purines were designed and synthesized. Although all compds. did not display PDE1 and PDE3 inhibitory activities, several heterocycle [i]-condensed purines strongly inhibited PDE4. Especially, dl-3,4-dipropyl-8-methyl-4,5,7,8-tetrahydro-1H- imidazo[2,1-i]purin-5-one (I) exhibited comparable PDE4 inhibitory activity (IC50=1.9 μM) to rolipram and denbufylline (DBF).

IT **156733-29-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocycle condensed purines from purine and pyrimidine derivs. and their activity as cAMP phosphodiesterase 4 isoenzyme inhibitors)

RN 156733-29-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:502824 CAPLUS Full-text
DOCUMENT NUMBER: 137:63122
TITLE: Preparation of purine derivatives or therapeutic use as phosphodiesterase IV inhibitors
INVENTOR(S): Chasin, Mark; Cavalla, David J.; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg

SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 285,473.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6413975	B1	20020702	US 2000-539571	20000331
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
HU 200200938	A2	20021028	HU 2002-938	20000331
JP 2001316314	A	20011113	JP 2000-136383	20000509
US 2003073834	A1	20030417	US 2002-62280	20020201

PRIORITY APPLN. INFO.:

US 1999-285473	A2	19990402
IN 1994-CA514	A1	19940630
US 1997-963054	A2	19971103
US 1997-875487	A2	19971113
US 1998-151949	A2	19980911
US 1998-210556	A2	19981211
US 1998-210557	A2	19981211
US 1999-227057	A2	19990107
US 1999-237638	A2	19990126
US 1999-361196	A2	19990726
US 2000-506624	A2	20000218
US 2000-539571	A2	20000331
US 2000-547575	A2	20000412
US 2000-547898	A2	20000412
US 2000-636146	A2	20000810
US 2000-724321	B1	20001128

OTHER SOURCE(S): MARPAT 137:63122
ED Entered STN: 04 Jul 2002
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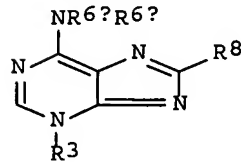

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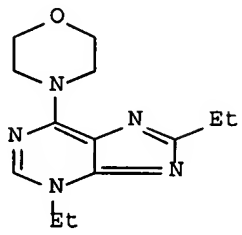


II

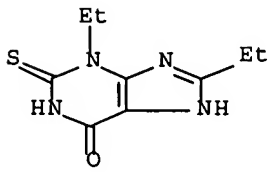
AB Purines, such as I [R3, R6a, R6b, R8 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase IV (PDE IV) inhibitors. Thus, 3,8-diethyl-6-morpholino- 3H-purine (II) was prepared by conversion of 3,8-diethyl-2-thioxanthine to 3,8-diethylhypoxanthine using 2N NaOH and nickel aluminum alloy, reaction of 3,8-diethylhypoxanthine to 3,8-diethyl-6-thiohypoxanthine using phosphorus pentasulfide in pyridine and, finally, reaction of 3,8-diethyl-6-

thiohypoxanthine with morpholine. The prepared purine derivs. were assayed for PDE IV inhibition.

IT **162278-04-8**, 3,8-Diethyl-2-thioxanthine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of purine derivs. for therapeutic use as phosphodiesterase IV inhibitors)

RN 162278-04-8 CAPLUS

CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:90055 CAPLUS Full-text
DOCUMENT NUMBER: 136:131252
TITLE: Cationic materials and methods for covalent bonding nucleic acids to high purity silica surfaces
INVENTOR(S): Lyles, Mark B.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008237	A2	20020131	WO 2001-US23079	20010720
WO 2002008237	A3	20021107		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001076023	A5	20020205	AU 2001-76023	20010720
US 2002103350	A1	20020801	US 2001-910697	20010720
US 6855817	B2	20050215		
EP 1305328	A2	20030502	EP 2001-953590	20010720
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US 2005148067	A1	20050707	US 2005-57440	20050214
PRIORITY APPLN. INFO.:			US 2000-220096P	P 20000721

US 2001-910697 A 20010720
WO 2001-US23079 W 20010720

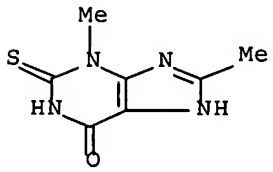
ED Entered STN: 01 Feb 2002

AB Surfaces containing high purity silica (silicon dioxide) exhibit high loading potential for nucleic acids. Formulations containing nucleic acids and materials which mask the electrostatic interactions between the nucleic acids and surfaces are disclosed. By masking the phosphate charges of the nucleic acids, undesired interactions may be minimized or eliminated, thereby allowing the covalent bonding of the nucleic acids to the surface to proceed. The use of such formulations addnl. minimizes nonspecific binding of the nucleic acids to the surface. Examples of materials to be included in such formulations include cations, xanthines, hexoses, purines, arginine, lysine, polyarginine, polylysine, and quaternary ammonium salts.

IT **91725-06-3**
RL: NUU (Other use, unclassified); USES (Uses)
(cationic materials and methods for covalent bonding nucleic acids to high purity silica surfaces)

RN 91725-06-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:413184 CAPLUS Full-text

DOCUMENT NUMBER: 135:251414

TITLE: Structural predictions of adenosine 2B antagonist affinity using molecular field analysis

AUTHOR(S): Song, Yuqing; Coupar, Ian M.; Iskander, Magdy N.

CORPORATE SOURCE: Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia

SOURCE: Quantitative Structure-Activity Relationships (2001), 20(1), 23-30
CODEN: QSARDI; ISSN: 0931-8771

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Jun 2001

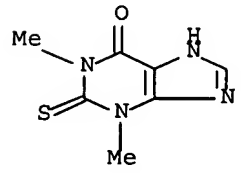
AB 3D structural evaluation of the adenosine 2B (A2B) antagonist binding site is the major aim for developing specific selective antagonists. In an attempt to deduce structural properties of the antagonist site, a pharmacophore model was developed using 85 known A2B antagonists. The mol. mechanics optimization methods were used to deduce the likely binding conformations of the antagonists at the binding site. Super-imposition of the antagonists was carried out using fit-atoms. This alignment was used to develop CoMFA models of the A2B antagonist binding site. The models possessed promising predictive ability as indicated by the high cross-validated correlation (q2 = 0.752, r2 = 0.982) and the prediction on the external test set. The analyses showed that

steric and electrostatic interactions contributed to A2B antagonist biol. activity equally. The hydrogen-bond donor nature of the 7-position of xanthine (1 .apprx. 68) and 3-position of alloxazine (83) was essential for the biol. activity. In addition, the presence of more neg. charges on the 1-N position of xanthine and 10-N position of alloxazine increases biol. activity. The bulky aromatic substitutions on the 8-position of xanthine compds. improve activity, while an alkyl substitution on the 1-position of alloxazine might enhance activity. The model generated from this investigation produced important structural requirements, which will be used to optimize the structural complementarity of the antagonists at the A2B binding site.

IT 6603-63-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural predictions of adenosine 2B antagonist affinity using mol. field anal.)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:136945 CAPLUS Full-text
DOCUMENT NUMBER: 134:193441
TITLE: Preparation of hypoxanthines and thiohypoxanthines as phosphodiesterase IV inhibitors
INVENTOR(S): Chasin, Mark; Hofer, Peter; Cavalla, David
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

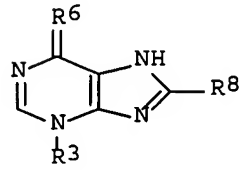
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001011967	A1	20010222	WO 2000-US21836	20000809

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

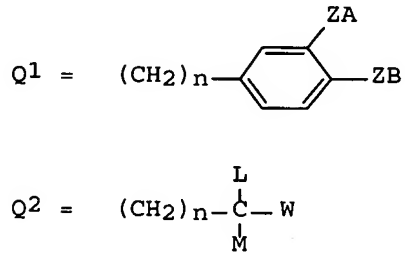
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

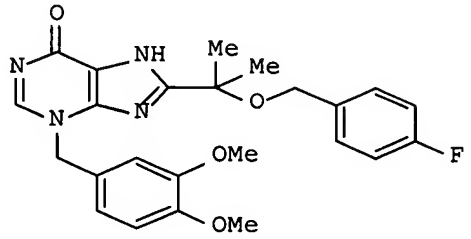
CA 2379356	A1	20010222	CA 2000-2379356	20000809
EP 1202628	A1	20020508	EP 2000-953925	20000809
EP 1202628	B1	20041013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506467	T	20030218	JP 2001-516330	20000809
AT 279113	T	20041015	AT 2000-953925	20000809
PRIORITY APPLN. INFO.:			US 1999-148623P P	19990812
			WO 2000-US21836 W	20000809

OTHER SOURCE(S): MARPAT 134:193441
ED Entered STN: 25 Feb 2001
GI



I





II

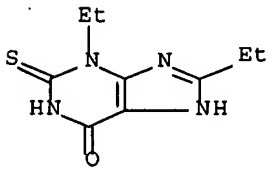
AB Title compds. (I) [wherein R3 and R8 = independently (cyclo)alkyl, alkenyl, alkynyl, Q1, or Q2; R6 = S or O; n = 0-1; Z = a bond, CH2, NH, O, or S; A and B can form a ring by adding 1-3 CH2 groups when Z = CH2, NH, O or S; and A and B are not in a ring when Z = a bond, wherein A and B = independently H, halo, (cyclo)alkyl, (cyclo)alkoxy, OH, or (un)substituted Ph, benzyl, or benzyloxy; L and M = independently H or Me; W = Q1, OH, (hetero)aryl, heterocyclyl, or (un)substituted benzyloxy] were prepared as selective phosphodiesterase (PDE) IV inhibitors. For example, amidation of 2-(4-fluorobenzyloxy)-2-methylpropionyl chloride with 5,6-diamino-1-(3,4-dimethoxybenzyl)-2-thiouracil using TEA in THF (20.4%), followed by cyclization with NaOH to form the 2-thioxanthine (79.1%) and treatment with Raney nickel in 1-propanol (67.2%), afforded the hypoxanthine (II). In assays measuring isolated PDE isoenzyme activity, II selectively inhibited PDE IV compared to PDE III and PDE V with IC50 values of 1.079 μM, 69.62 μM, and 35.80 μM, resp. As a result, I are expected to induce the desirable anti-asthmatic effects associated with PDE IV inhibition without causing the undesirable cardiovascular stimulation associated with PDE III inhibition (no data). I are useful in the treatment of asthma, allergies, inflammation, depression, dementia, and other disease states associated with abnormally high physiol. levels of cytokine (no data).

IT **162278-04-8**, 3,8-Diethyl-2-thioxanthine

RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of hypoxanthine and thiohypoxanthine phosphodiesterase IV inhibitors from thiouracils and acyl halides and anhydrides)

RN 162278-04-8 CAPLUS

CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:725418 CAPLUS Full-text

DOCUMENT NUMBER: 133:296324

TITLE: Synthesis and phosphodiesterase IV inhibition activity of purine derivatives

INVENTOR(S): Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig, Andre; Wintergest, Peter

PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg

SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

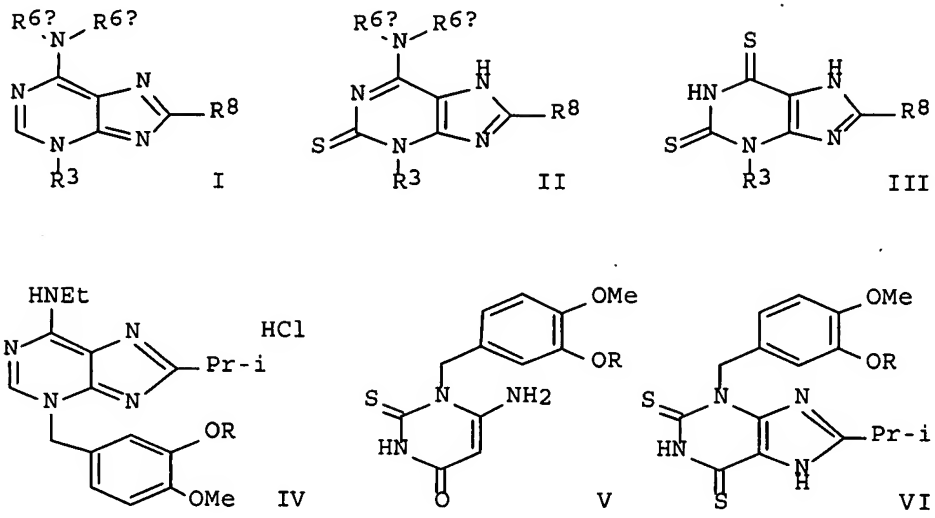
FAMILY ACC. NUM. COUNT: 21

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059449	A2	20001012	WO 2000-US8525	20000331
WO 2000059449	A3	20010104		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
CA 2367143	A1	20001012	CA 2000-2367143	20000331
EP 1169321	A2	20020109	EP 2000-919929	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200200938	A2	20021028	HU 2002-938	20000331
JP 2002541078	T	20021203	JP 2000-609014	20000331
BR 2000011182	A	20030610	BR 2000-11182	20000331
JP 2001316314	A	20011113	JP 2000-136383	20000509

PRIORITY APPLN. INFO.: US 1999-285473 A 19990402
IN 1994-CA514 A1 19940630
WO 2000-US8525 W 20000331

OTHER SOURCE(S): MARPAT 133:296324
ED Entered STN: 13 Oct 2000
GI

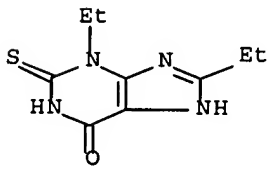


AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH2)5) was prepared by etherification of isovanilline with cyclopentanol, oximation, reduction to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC50 of IV against phosphodiesterase IV inhibition was 0.32 μM. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

IT **162278-04-8**, 3,8-Diethyl-2-thioxanthine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of purine derivs. as phosphodiesterase IV inhibitors)

RN 162278-04-8 CAPLUS

CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)

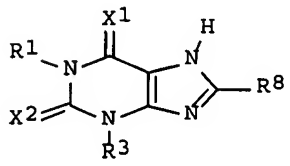


L9 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:113098 CAPLUS Full-text
DOCUMENT NUMBER: 132:151831
TITLE: Preparation of thioxanthines as PDE IV inhibitors
INVENTOR(S): Cavalla, David; Hofer, Peter; Chasin, Mark
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 476,262, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6025361	A	20000215	US 1997-860674	19970929
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
CA 2206804	A1	19960620	CA 1995-2206804	19951212
CA 2206804	C	20020319		
WO 9618400	A1	19960620	WO 1995-US16724	19951212
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IN 1995CA01665	A	20050304	IN 1995-CA1665	19951218
US 5977119	A	19991102	US 1997-931849	19970915
US 6268373	B1	20010731	US 1999-361196	19990726

PRIORITY APPLN. INFO.:
US 1994-354664 B2 19941213
US 1995-476262 B2 19950607
WO 1995-US16724 W 19951212
IN 1994-CA514 A1 19940630
US 1997-860674 A1 19970929

OTHER SOURCE(S): MARPAT 132:151831
ED Entered STN: 17 Feb 2000
GI



I

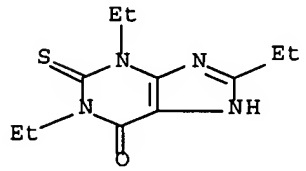
AB Title compds. [I; R1,R3,R8 = alkyl or aryl(alkyl); 1 of X1,X2 = S and the other = O or S] were prepared Thus, 5,6-diamino-1,3-diethyl-2-thiouracil was

N-acylated by cyclopropanecarbonyl chloride and the cyclized product treated with P4S10 to give I (R1 = R3 = Et, X1 = X2 = S). Data for biol. activity of I were given.

IT **257939-27-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thioxanthines as PDE IV inhibitors)

RN 257939-27-8 CAPLUS

CN 6H-Purin-6-one, 1,3,8-triethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 186 THERE ARE 186 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:412389 CAPLUS Full-text

DOCUMENT NUMBER: 131:179928

TITLE: 1,3-Dialkylxanthine derivatives having high potency as antagonists at human A2b adenosine receptors

AUTHOR(S): Jacobson, Kenneth A.; Ijzerman, Ad P.; Linden, Joel

CORPORATE SOURCE: Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA

SOURCE: Drug Development Research (1999), 47(1), 45-53
CODEN: DDREDK; ISSN: 0272-4391

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

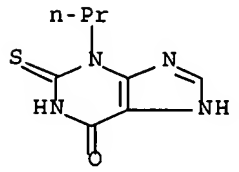
ED Entered STN: 05 Jul 1999

AB The structure-activity relationships (SAR) of alkylxanthine derivs. as antagonists at the recombinant human adenosine receptors were explored in order to identify selective antagonists of A2B receptors. The effects of lengthening alkyl substituents from Me to Bu at 1- and 3-positions and addnl. substitution at the 7- and 8-positions were probed. Ki values, determined in competition binding in membranes of HEK-293 cells expressing A2B receptors using 125I-ABOPX (125I-3-(4-amino-3-iodobenzyl)-8-(phenyl-4- oxyacetate)-1-propylxanthin e), were approx. 10 to 100 nM for 8-phenylxanthine functionalized congeners. Xanthines containing 8-aryl, 8-alkyl, and 8-cycloalkyl substituents, derivs. of XCC (8-[4-[[[carboxy]methyl]oxy]phenyl]-1,3-dipropylxanthine) and XAC (8-[4-[[[[(2-amino-ethyl)amino]carbonyl]methyl]-oxy]phenyl]-1,3- dipropylxanthine), containing various ester and amide groups, including L- and D-amino acid conjugates, were included. Enprofylline was 2-fold more potent than theophylline in A2B receptor binding, and the 2-thio modification was not tolerated. Among the most potent derivs. examined were XCC, its hydrazide and aminoethyl and fluoroethyl amide derivs., XAC, N-

hydroxyethyl-XAC, and the L-citrulline and D-p-aminophenylalanine conjugates of XAC. An N-hydroxysuccinimide ester of XCC (XCC-NHS, MRS 1204) bound to A2B receptors with a Ki of 9.75 nM and was the most selective (at least 20-fold) in this series. In a functional assay of recombinant human A2B receptors, four of these potent xanthines were shown to fully antagonize the effects of NECA-induced stimulation of cAMP accumulation.

IT 156733-29-8
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(1,3-Dialkylxanthine derivs. having high potency as antagonists at human A2b adenosine receptors)

RN 156733-29-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)

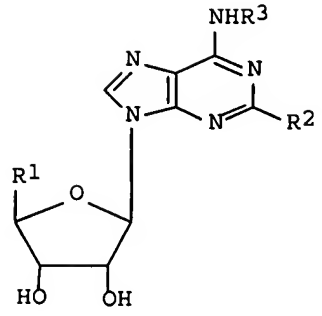


REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:441960 CAPLUS Full-text
DOCUMENT NUMBER: 129:109311
TITLE: Preparation of nucleoside uronamides as A3 adenosine receptor agonists
INVENTOR(S): Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Van Galen, Philip J. M.; Von Lubitz, Dag K. J. E.; Jeong, Heaok Kim
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 54 pp., Cont.-in-part of U. S. Ser. No. 163,324, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773423	A	19980630	US 1994-274628	19940713
US 5688774	A	19971118	US 1995-396111	19950228
PRIORITY APPLN. INFO.:			US 1993-91109	B2 19930713
			US 1993-163324	B2 19931206
			US 1994-274628	A2 19940713

OTHER SOURCE(S): MARPAT 129:109311
ED Entered STN: 17 Jul 1998
GI



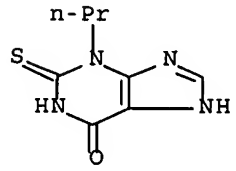
I

AB The present invention provides N6-benzyladenosine-5'-N-uronamide and related substituted compds. I (R1 = amide; R2 = halo, amino, alkenyl, alkynyl, thio, alkylthio; R3 = S-1-phenylethyl, Bn, phenylethyl), particularly those containing substituents on the benzyl and/or uronamide groups, and modified xanthine ribosides, as well as pharmaceutical compns. containing such compds. The present invention also provides a method of selectively activating an A3 adenosine receptor in a mammal, which method comprises acutely or chronically administering to a mammal in need of selective activation of its A3 adenosine receptor a therapeutically effective amount of a compound which binds with the A3 receptor so as to stimulate an A3 receptor-dependent response. Thus, N6-(3- iodobenzyl)adenosine was prepared tested for its affinity in binding at rat brain A1, A2, A3 adenosine receptors (Ki = 9.5-220.0 nM).

IT **156733-29-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nucleoside uronamides as A3 adenosine receptor agonists)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



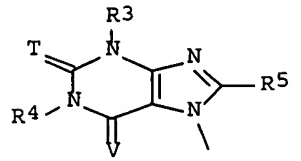
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:331961 CAPLUS Full-text
DOCUMENT NUMBER: 126:305588
TITLE: Preparation of 4-(dioxopurinylmethyl)phenylacetates and analogs as hypolipemics
INVENTOR(S): Connell, Richard; Goldmann, Siegfried; Mueller, Ulrich; Lohmer, Stefan; Bischoff, Hilmar; Denzer, Dirk; Gruetzmann, Rudi; Wohlfeil, Stefan
PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 764647	A1	19970326	EP 1996-114577	19960912
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 19535504	A1	19970327	DE 1995-19535504	19950925
US 5714494	A	19980203	US 1996-710503	19960918
JP 09216884	A	19970819	JP 1996-267691	19960919
CA 2186086	A1	19970326	CA 1996-2186086	19960920

PRIORITY APPLN. INFO.: DE 1995-19535504 A 19950925
OTHER SOURCE(S): MARPAT 126:305588
ED Entered STN: 24 May 1997
GI

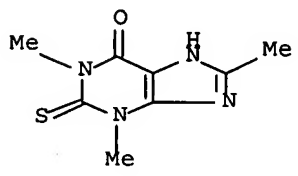


II

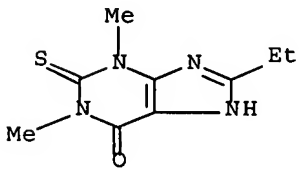
AB RCH2ZCHR1C(:L)R2 [I; R = xanthine moiety, e.g., II; R1 = H, (cyclo)alkyl, Ph, heterocyclyl, etc.; R2 = OH, SH, alkoxy, (di)alkylamino, etc.; R3,R4 = H, alkyl, aryl, etc.; R5 = H, halo, alkyl, aryl, etc.; L,T,V = O or S; Z = (un)substituted 1,4-phenylene] were prepared Thus, 5,6-diamino-1,3-dimethyluracil was cyclocondensed with 4-MeC6H4CHO and the product N-alkylated by 4-(BrCH2)C6H4CHR1CO2CMe3 (R1 = cyclopentyl)(preparation given) to give 4-(RCH2)C6H4CHR1CO2CMe3 (R = II, R1 = cyclopentyl, R3 = R4 = Me, R5 = C6H4Me-4, T = V = O). Data for biol. activity of I were given.

IT **19673-55-3P 189215-37-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-(dioxopurinylmethyl)phenylacetates and analogs as hypolipemics)

RN 19673-55-3 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,8-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 189215-37-0 CAPLUS
CN 6H-Purin-6-one, 8-ethyl-1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:492020 CAPLUS Full-text
DOCUMENT NUMBER: 122:239459
TITLE: Preparation of purines, isoguanines, and dithioxanthines as phosphodiesterase-IV inhibitors
INVENTOR(S): Cavalla, David; Hofer, Peter; Gehrig, Anddre; Wintergest, Peter
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

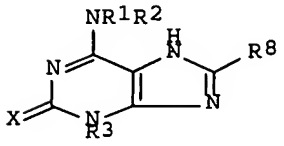
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500516	A1	19950105	WO 1994-GB1334	19940621
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2165433	A1	19941223	CA 1994-2165433	19940621
CA 2165433	C	20020528		
AU 9469771	A	19950117	AU 1994-69771	19940621
AU 683270	B2	19971106		
EP 705265	A1	19960410	EP 1994-918456	19940621
EP 705265	B1	19990728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1125445	A	19960626	CN 1994-192521	19940621
CN 1045778	B	19991020		
HU 74176	A2	19961128	HU 1995-3545	19940621
JP 09500376	T	19970114	JP 1995-502570	19940621
JP 3350550	B2	20021125		
EP 916672	A1	19990519	EP 1999-100735	19940621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 916673	A1	19990519	EP 1999-100736	19940621
EP 916673	B1	20030129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 182593	T	19990815	AT 1994-918456	19940621

ES 2137371	T3	19991216	ES 1994-918456	19940621
NZ 328914	A	20000825	NZ 1994-328914	19940621
AT 231863	T	20030215	AT 1999-100736	19940621
ZA 9404463	A	19950217	ZA 1994-4463	19940622
IN 177888	A1	19970222	IN 1994-CA514	19940630
TW 418208	B	20010111	TW 1994-83107047	19940802
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
FI 9506168	A	19960201	FI 1995-6168	19951221
NO 9505219	A	19960222	NO 1995-5219	19951221
BG 62933	B1	20001130	BG 1995-100258	19951227
US 5939422	A	19990817	US 1996-578580	19960408
US 6310205	B1	20011030	US 1999-237638	19990126
US 6294541	B1	20010925	US 1999-418330	19991014
US 6319928	B1	20011120	US 1999-418331	19991014

PRIORITY APPLN. INFO.:

GB 1993-12853	A	19930622
EP 1994-918456	A3	19940621
NZ 1994-267468	A1	19940621
WO 1994-GB1334	W	19940621
IN 1994-CA514	A1	19940630
US 1996-578580	A2	19960408
US 1996-659767	A1	19960606
US 1997-69371P	P	19971212
US 1998-200615	B2	19981130
US 1998-210556	A2	19981211
US 1999-285473	A1	19990402

OTHER SOURCE(S): MARPAT 122:239459
ED Entered STN: 18 Apr 1995
GI



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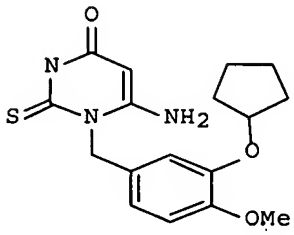
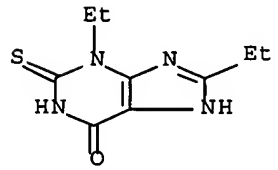


II

AB Title compds. [e.g., I; R1-R3,R8 = H, (cyclo)alkyl, (hetero)aryl, etc.; NR1R2 = heterocyclyl] were prepared Title compds. have bronchial and tracheal relaxation and/or antiinflammatory activity. Thus, isovanillin was converted in 5 steps to 3,4-(HO)(MeO)C6H3CH2NHCSNH2 which was cyclocondensed with NCCH2CO2Et to give thiouracil II. The latter was converted in 3 steps to 6-amino-1-(3-cyclopentyloxy-4-methoxybenzyl)-5- isobutyrylamino-2-thiouracil which was cyclized and the product converted in 4 steps to I.HCl (R1 = Et, R2 = H, R3 = 3-cyclopentyloxy-4- methoxybenzyl, R8 = CHMe2)(III). III gave 64% inhibition of ovalbumin-induced bronchoalveolar eosinophil production in guinea pigs at 5mg/kg i.p.

IT **162278-04-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of purines, isoguanines, and dithioxanthines as

phosphodiesterase-IV inhibitors)
RN 162278-04-8 CAPLUS
CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



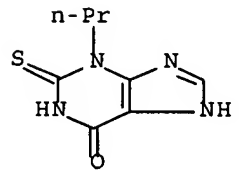
L9 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:500054 CAPLUS Full-text
DOCUMENT NUMBER: 121:100054
TITLE: A binding site model and structure-activity relationships for the rat A3 adenosine receptor
AUTHOR(S): van Galen, Philip J. M.; van Bergen, Andrew H.; Gallo-Rodriguez, Carola; Melman, Neli; Olah, Mark E.; Ijzerman, Ad P.; Stiles, Gary L.; Jacobson, Kenneth A.
CORPORATE SOURCE: Lab. Bioorganic Chem., Natl. Inst. Diabetes, Digestive and Kidney Diseases, Bethesda, MD, 20892, USA
SOURCE: Molecular Pharmacology (1994), 45(6), 1101-11
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 Sep 1994
AB A novel adenosine receptor, the A3 receptor, has recently been cloned. The authors have systematically investigated the hitherto largely unexplored structure-activity relationships (SARs) for binding at A3 receptors, using 125I-N6-2-(4-aminophenyl)ethyladenosine as a radioligand and membranes from Chinese hamster ovary cells stably transfected with the rat A3-cDNA. As is the case for A1 and A2a receptors, substitutions at the N6 and 5' positions of adenosine, the prototypic agonist ligand, may yield fairly potent compds. However, the highest affinity and A3 selectivity is found for N6,5'-disubstituted compds., in contrast to A2 and A2a receptors. Thus, N6-benzyladenosine-5'-N-ethylcarboxamide is highly potent (Ki, 6.8 nM) and moderately selective (13- and 14-fold vs. A1 and A2a). The N6 region of the A3 receptor also appears to tolerate hydrophilic substitutions, in sharp contrast to the other subtypes. Potencies of N6,5'-disubstituted compds. in inhibition of adenylate cyclase via A3 receptors parallel their high affinity in the binding assay. None of the typical xanthine or nonxanthine (A1/A2) antagonists tested show any appreciable affinity for rat A3 receptors. 1,3-Dialkylxanthines did not antagonize the A3 agonist-induced inhibition of adenylate cyclase. A His residue in helix 6 that is absent in A3 receptors but present in A1/A2 receptors may be causal in this respect. In a mol. model for the rat A3 receptor, this mutation, together with an increased bulkiness of residues surrounding the ligand, make antagonist binding unfavorable when compared with a previously developed A1 receptor model. Second, this A3 receptor model predicted similarities with A1 and A2 receptors in the binding requirements for the ribose moiety and that xanthine-7-ribosides would bind to rat A3 receptors. This hypothesis was supported exptl. by the moderate affinity (Ki, 6 μM) of 7-riboside of 1,3-dibutylxanthine, which appears to be a partial agonist at rat A3 receptors. The model presented here which is

consistent with the detailed SAR found in this study, may serve to suggest future chemical modification, site-directed mutagenesis, and SAR studies to further define essential characteristics of the ligand-receptor interaction and to develop even more potent and selective A3 receptor ligands.

IT **156733-29-8**
RL: BIOL (Biological study)
(adenosine A1 and A2a and A3 receptors affinity for, mol. structure in relation to)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:644995 CAPLUS Full-text

DOCUMENT NUMBER: 117:244995

TITLE: Approach to an adenosine pharmacophore by molecular modeling

AUTHOR(S): Neuwels, M.

CORPORATE SOURCE: UCB Sect. Pharm., Chemin Foriest, Braine-l-Alleud, B-1420, Belg.

SOURCE: Journal de Pharmacie de Belgique (1992), 47(4), 351-63
CODEN: JPBEAJ; ISSN: 0047-2166

DOCUMENT TYPE: Journal

LANGUAGE: French

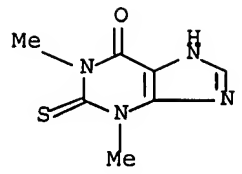
ED Entered STN: 26 Dec 1992

AB The selective development of adenosine A1 antagonists was carried out in 2 steps. First an A1 pharmacophore common to various known chemical families was determined in order to permit the design of new chemical skeletons; then a predictive modeling of affinities was carried out to select new potential ligands. The mol. modeling was done on 6 different chemical families (triazoloquinoxalines, adenines, xanthines, pyrazolopyrimidinones, triazoloquinazolines, and imidazoquinolines), and a search for a common superimposition was carried out. Starting from the different superpositions obtained, a CoMFA study (QSAR-3D) allowed the building of predictive models for A1 receptor affinity. The theor. preferred superposition proved to be the best, as it was able to correctly predict the activities of new ligands.

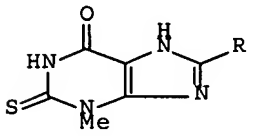
IT **6603-63-0**
RL: BIOL (Biological study)
(in mol. modeling of adenosine receptor pharmacophore)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:426495 CAPLUS Full-text
DOCUMENT NUMBER: 117:26495
TITLE: Facile and general synthesis of 8-substituted 2-(methylthio)purin-6-ones
AUTHOR(S): Nagamatsu, Tomohisa; Yamasaki, Hiroo
CORPORATE SOURCE: Fac. Pharm. Sci., Okayama Univ., Tsushima, 700, Japan
SOURCE: Heterocycles (1992), 33(2), 775-90
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:26495
ED Entered STN: 26 Jul 1992
GI



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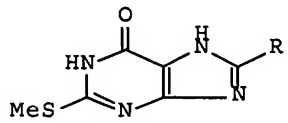
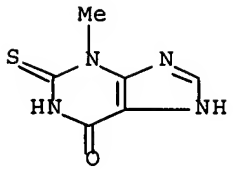


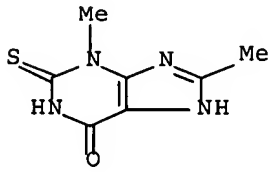
II

AB 3-Methyl-6-oxo-2-thioxo-1,2,3,6-tetrahydropurines [I; R = H, alkyl, (un)substituted Ph] were synthesized by oxidative cyclization of 5,6-diamino-1-methyl-2-thiouracil-RCHO reaction products or 6-amino-5-(benzylideneamino)-1-methyl-2-thiouracils in the presence of di-Et azodicarboxylate (DEAD). In addition, the oxidative cyclization of 4-amino-5-(benzylideneamino)-3-methyl-2-(methylthio)pyrimidin-6(3H)-ones in the presence of DEAD gave 8-aryl-3-methyl-2-(methylthio)-6-oxo-3,6- dihydropurines, which were identical with the compds. prepared by methylation of I. 2-(Methylthio)-6-oxo-1,6-dihydropurines [II; R = H, alkyl, (un)substituted Ph] were synthesized from 4,5-diamino-2-(methylthio)pyrimidin-6(1H)-one or 4-amino-5-(benzylideneamino)-2-(methylthio)pyrimidin-6(1H)-ones in a similar manner as above.

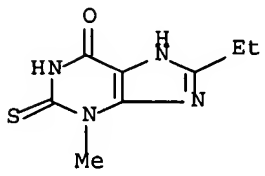
IT **28139-02-8P 91725-06-3P 103289-69-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)
RN 28139-02-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



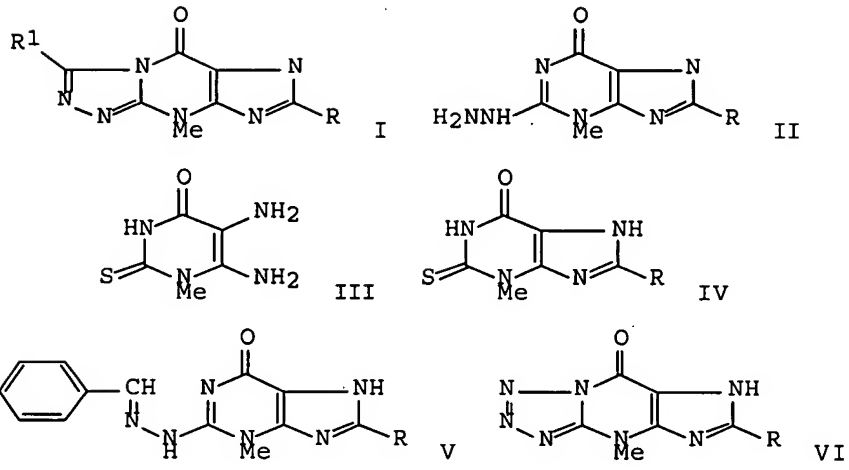
RN 91725-06-3 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 103289-69-6 CAPLUS
CN 6H-Purin-6-one, 8-ethyl-1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:478896 CAPLUS Full-text
DOCUMENT NUMBER: 105:78896
TITLE: Syntheses of 4-methyl-s-triazolo[4,3-a]purin-9(4H)-ones and tetrazolo[1,5-a]purin-9(4H)-ones as aza analogs of "Y" bases
AUTHOR(S): Nagamatsu, Tomohisa; Ukai, Masayoshi; Yoneda, Fumio; Brown, Desmond J.
CORPORATE SOURCE: Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, 862, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1985), 33(8), 3113-21
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:78896
ED Entered STN: 06 Sep 1986
GI

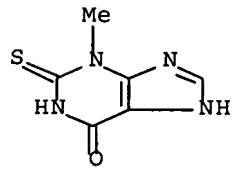


AB 4-Methyl-s-triazolo[4,3-a]purin-9(4H)-ones I (R = H, Me, Et, Ph; R1 = H, Me, Et) were prepared by the cyclocondensation of purin-6(3H)-ones II (R = same) with the appropriate R1C(OEt)3. II were prepared by cyclizing pyrimidine III with RC(OEt)3 and treating the resulting thioxanthines IV with NH2NH2. I [R = Me, Et, Ph; R1 = p-R2C6H4 (R2 = H, Me, Cl, OMe)] were prepared by the condensation of the appropriate II with p-R2C6H4CHO, followed by the oxidative cyclization of the resulting arylidenehydrazine derivs. V. I (R = Me, Et; R1 = SH, SMe, SEt, SCH2CONH2) were also prepared Tetrazolo[1,5-a]purin-9(4H)-ones VI (R = H, Me, Et, Ph) were prepared by treating the corresponding II with NaNO2/HCl.

IT **28139-02-8P 91725-06-3P 103289-69-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrazine)

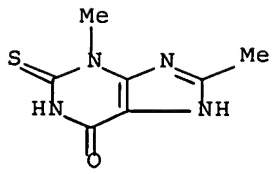
RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)

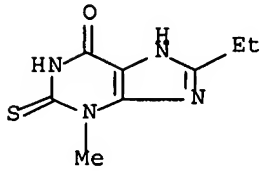


RN 91725-06-3 CAPLUS

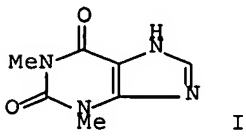
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 103289-69-6 CAPLUS
CN 6H-Purin-6-one, 8-ethyl-1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:119142 CAPLUS Full-text
DOCUMENT NUMBER: 98:119142
TITLE: Alkylxanthines as adenosine receptor antagonists and membrane phosphodiesterase inhibitors in central nervous tissue: evaluation of structure-activity relationships
AUTHOR(S): Wu, P. H.; Phillis, J. W.; Nye, M. J.
CORPORATE SOURCE: Coll. Med., Univ. Saskatchewan, Saskatoon, SK, Can.
SOURCE: Life Sciences (1982), 31(25), 2857-67
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



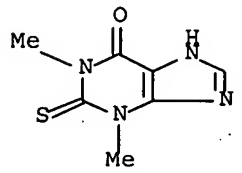
I

AB A series of alkylxanthines were examined as antagonists of the adenosine [58-61-7] A1-receptor in rat brain synaptosomal membranes and as inhibitors of membrane phosphodiesterase [9025-82-5]. Structure-activity relations showed that the addition of certain substituting groups at position 8 of the theophylline mol. produced mol. structures which generally favored adenosine receptor antagonism. This is evident from the potency order of 8-substituted

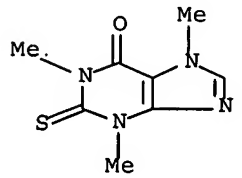
theophyllines as adenosine receptor antagonists: 8-(p-bromophenyl)theophylline [63325-99-5], 8-(p- methylphenyl)theophylline [57196-70-0], 8-phenyltheophylline [961-45-5] and 8-(p-chlorophenyltheophylline [29064-02-6], 8- (methoxyphenyl)theophylline [84942-90-5] > 8-(dimethylaminophenyl)theophylline [54013-59-1] > 8-benzyltheophylline [2879-15-4] > theophylline (I) [58-55-9]. The order of potency for inhibition of brain membrane phosphodiesterase was: 1,3-dimethyl-2,6- dithioxopurine [6501-94-6] > methylxanthines > 8-substituted theophyllines. 8-Substituted theophyllines may be selective in their activity as adenosine receptor antagonists, whereas an increase in lipid solubility by substitution at the 1, 2, 3, and 6 positions of the purine ring may result in an increase in phosphodiesterase inhibition.

IT **6603-63-0 24049-32-9**
RL: BIOL (Biological study)
(adenosine receptor and phosphodiesterase of synaptosome membrane response to, alkylxanthines effect on)

RN 6603-63-0 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)

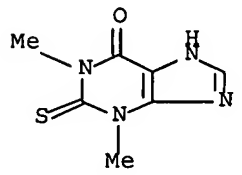


RN 24049-32-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)

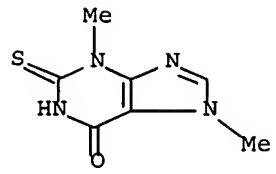


L9 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:435269 CAPLUS Full-text
DOCUMENT NUMBER: 95:35269
TITLE: Adenosine antagonism by purines, pteridines, and benzopteridines in human fibroblasts
AUTHOR(S): Bruns, Robert F.
CORPORATE SOURCE: Dep. Neurosci., Univ. California, La Jolla, CA, 92093, USA
SOURCE: Biochemical Pharmacology (1981), 30(4), 325-33
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

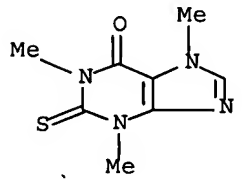
ED Entered STN: 12 May 1984
AB Testing of >100 purine bases and structurally related heterocycles as adenosine (I) [58-61-7] antagonists in VA13 fibroblasts (determined by cAMP increase) yielded 3 families of I antagonists: xanthines, benzo[g]pteridines, and 9-substituted adenines. For the xanthines, the optimal group at the 1-position was Bu (5-fold improvement vs. Me), at the 7-position was 2-chloroethyl (5-fold improvement vs. H), and at the 8-position was p-bromophenyl (100-fold improvement vs. H). The receptors apparently had butyl- and phenyl-sized pockets at the 1- and 8-positions, resp., since compds. with larger groups had greatly reduced activity.
IT **6603-63-0**
RL: BIOL (Biological study)
(adenosine receptor of fibroblast antagonism by)
RN 6603-63-0 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



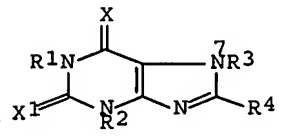
L9 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:37755 CAPLUS Full-text
DOCUMENT NUMBER: 88:37755
TITLE: Reaction of iodides of 2-methylthio-N,N'-dimethyl-and -N,N',N''-trimethylhypoxanthiniums and their 8-aza analogs during heating and alkylation
AUTHOR(S): Muravich-Aleksandr, Kh. L.; Kolesova, M. B.; Mezhonova, S. S.; Smirnova, N. V.
CORPORATE SOURCE: USSR
SOURCE: Zhurnal Organicheskoi Khimii (1977), 13(8), 1780-7
CODEN: ZORKAE; ISSN: 0514-7492
DOCUMENT TYPE: Journal
LANGUAGE: Russian
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB Thermal transformation of hypoxanthinium iodide I 75 min at 195° gave 13% II (R = Me), 5% III (R = Me) 41% thione IV (R = Me), and 41% IV (R = H). Analogously II (R = Me) 75 min at 225° gave 54% starting material, 19% III (R = Me) and 27% IV (R = Me); II (R = H) under identical conditions gave 24% II (R = Me), 36% starting material, 7% III (R = H), 11% III (R = Me), 17% IV (R = H), and 5% IV (R = Me).
IT **19373-97-8P 24049-32-9P**
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in thermal transformations of hypoxanthinium derivs.)
RN 19373-97-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 24049-32-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:453218 CAPLUS Full-text
DOCUMENT NUMBER: 87:53218
TITLE: 6-Sulfinyl derivatives of xanthines
AUTHOR(S): Bergmann, Felix; Frank, Arie; Weiler-Feilchenfeld, Hanna; Tamir, Ilana
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
SOURCE: Journal of Organic Chemistry (1977), 42(14), 2470-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI

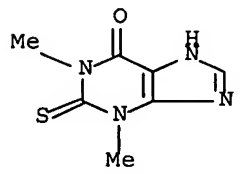


I, X=S
II, X=SO

AB 6-Thiopurines I (R1 = R4 = H, R2 = R3 = Me, X1 = O; R1 = R2 = Me, R3 = R4 = H, X1 = O, S; R1 = R2 = Me, R3 = H, R4 = Ph, X1 = O, S) are oxidized by H2O2 or by BzOOH to 6-sulfinylpurines II. Only theophylline derivs. of these unstable II were obtained in pure form. The isomers formed have the 6-sulfinyl group directed toward the 7-NH due to stabilization by an intramol. H bridge. Their structure has been derived from dipole moments and from the chemical shift of

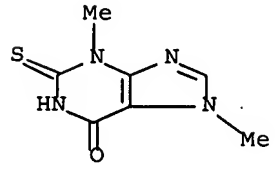
the 1-Me substituent. The 2-thiocarbonyl group in 2-thiotheophyllines is not attacked by the oxidants used, which convert 6-selenoxanthines to the corresponding xanthines.

IT **6603-63-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of)
RN 6603-63-0 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)

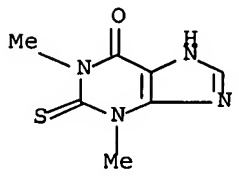


L9 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1974:82889 CAPLUS Full-text
DOCUMENT NUMBER: 80:82889
TITLE: Tautomerism, ionization, and methylation of 2-(methylthio)- and 2,8-bis(methylthio)hypoxanthines
AUTHOR(S): Reichman, Uri; Bergmann, Felix; Lichtenberg, Dov
CORPORATE SOURCE: Dep. Pharmacol., Heb. Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1973), (22), 2647-55
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB Anion formation in the title compds. occurred first at N-1 and then at N-7(9). Protonation involved the imidazole ring except for 3-Me derivs. which were protonated at N-1. Methylation of 3-Me derivs. of the title compds. occurred preferentially at N-7. The formation of cations of partial structure [RNC(SMe)NMe]+ was followed by S-demethylation.

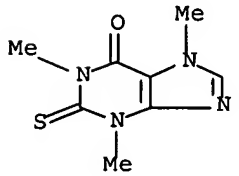
IT **19373-97-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 19373-97-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



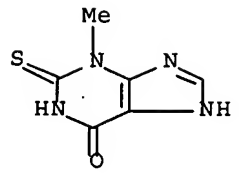
L9 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:434696 CAPLUS Full-text
DOCUMENT NUMBER: 75:34696
TITLE: Nuclear magnetic resonance spectra of xanthines and thioxanthines
AUTHOR(S): Bergmann, F.; Lichtenberg, D.; Neiman, Z.
CORPORATE SOURCE: Hadassah Med. Sch., Heb. Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society [Section] C: Organic (1971), (10), 1939-41
CODEN: JSOOAX; ISSN: 0022-4952
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB The NMR signal of the 8-H in xanthines is shifted downfield more strongly by introduction of a 2- than of a 6-thioxo group. The signals of N-Me groups are also shifted to lower field, but the effect depends strictly on the distance between the Me and the thioxo. In 2-thioxanthines, the displacement decreases in the order 1-Me = 3-Me > 7-Me, and in 6-thioxanthines the sequence is 1-Me > 7-Me > 3-Me > 9-Me.
IT **6603-63-0 24049-32-9 28139-02-8**
RL: PRP (Properties)
(nuclear magnetic resonance of)
RN 6603-63-0 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



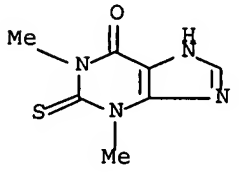
RN 24049-32-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



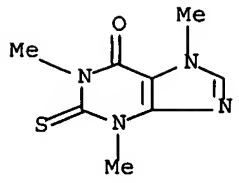
RN 28139-02-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



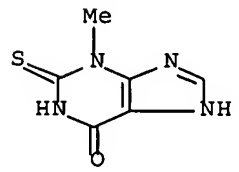
L9 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:403341 CAPLUS Full-text
DOCUMENT NUMBER: 73:3341
TITLE: Dipole moments and electronic structure of some xanthine and thioxanthine derivatives
AUTHOR(S): Weiler-Feilchenfeld, Hannah; Neiman, Zohar
CORPORATE SOURCE: Dep. Org. Chem., Hebrew Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society [Section] B: Physical Organic (1970), 4, 596-8
CODEN: JCSPAC; ISSN: 0045-6470
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB The dipole moments and uv absorption spectra of caffeine, theophylline, and their 2-thio-, 6-thio- and 2,6-dithio derivs. were measured. From the differences between the moments of these compounds it can be deduced that the C:S group moment is higher by 1.1 D than that of C:O; the direction of the moment of caffeine forms an angle of 96° counterclockwise with the C(4) → C(5) axis, in good agreement with theoretical predictions.
IT **6603-63-0 24049-32-9**
RL: PRP (Properties)
(dipole moment of)
RN 6603-63-0 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 24049-32-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)

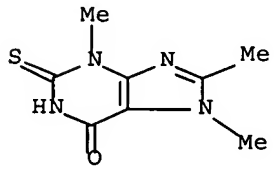


L9 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:126337 CAPLUS Full-text
DOCUMENT NUMBER: 72:126337
TITLE: Mass spectrometric investigations of heterocyclic compounds. V. Fragmentation of some purines
AUTHOR(S): Heiss, Juergen; Zeller, Klaus P.; Voelter, Wolfgang
CORPORATE SOURCE: Chem. Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Organic Mass Spectrometry (1970), 3(2), 181-90
CODEN: ORMSBG; ISSN: 0030-493X
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 12 May 1984
AB The mass spectra of 9 purines are discussed. The xanthine purines eliminate HNCO and CO consecutively, whereas 3-methylhypoxanthine loses HCN and CO. In the case of 3-methylxanthine, an ion is formed whose stabilization by rearrangement is discussed. The fragmentation patterns of 3-methyl-2-thioxanthine and 3-methylthiohypo xanthine are different from those of the corresponding O analogs. 6-(Methylthio)purine and 6-methoxypurine eliminate HCS· or HCO ·, resp. For the latter reaction a mechanism is suggested.
IT **28139-02-8**
RL: PRP (Properties)
(mass spectrum of)
RN 28139-02-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



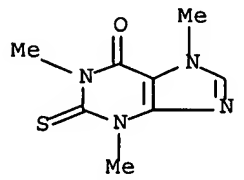
L9 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:512889 CAPLUS Full-text
DOCUMENT NUMBER: 71:112889
TITLE: Syntheses in the purine series. XX. Effect of chloride compounds of phosphorus on 8-methyltheobromine
AUTHOR(S): Gutorov, L. A.; Golovchinskaya, E. S.
CORPORATE SOURCE: Vses. Nauch.-Issled. Khim.-Farm. Inst. im. Ordzhonikidze, Moscow, USSR

SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1969), 3(7), 4-10
CODEN: KHFZAN; ISSN: 0023-1134
DOCUMENT TYPE: Journal
LANGUAGE: Russian
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB To 3 g. 8-methyltheobromine (I) in 15 ml. POCl3 was added 6.45 g. PCl5 and the mixture boiled 4 hrs. to give 0.8 g. 2,6-dichloro-7,8-dimethylpurine (II), m. 149-50° (H2O). From I were prepared III (X = Cl) (IIIa) and IV (X = Cl) (IVa), which were converted to other derivs. Thus, 60 g. I was boiled 4-6 hrs. in 400 ml. POCl3, the solution concentrated and added to 900 g. ice and 700-800 g. NaHCO3, the mixture filtered, and the residue extracted with CHCl3 to give 28-9 g. IIIa, m. 235-8° (PhMe). The aqueous filtrate was extracted with CHCl3 and the extract concentrated to 50 ml. to give .apprx.68% IVa, m. 241-2° (PhMe). III (X = OEt), m. 176° (C6H6), was obtained in 43% yield when NaOEt solution (from 0.2 g. Na and 10 ml. EtOH) was added dropwise to 1.8 g. IIIa in 5 ml. EtOH. Similarly, IVa gave 43% IV (X = OEt), m. 270-1° (alc.). IIIa (0.35 g.) was boiled 1.5 hrs. in 10 ml. 25% NH4OH and the product filtered off, dissolved in N HCl and precipitated with 2N NaOH to give 63% III (X = NH2), m. 338-40°. IV (X = NH2), m. 311-12°, 82.6%, was obtained similarly. IIIa (1.7 g.) in 10 ml. 30% NHMe2 gave 79% III (X = NMe2) 1.4 g., m. 168-9° (C6H6). Similarly obtained was 72% IV (X = NMe2), m. 196-200° (C6H6). III (X = SH)(IIIb), m. 277-9° (alc.), 95%, and IV (X = SH) (IVb), m. 314-16° (HCONMe2), 99%, were similarly obtained from alc. thiourea. IIIb and IVb were converted, resp., to III (X = SMe), m. 223-5° (C6H6), 74%, and IV (X = SMe), m. 252-3° (alc.), .apprx.100%, by shaking their solns. in N NaOH with MeI and extracting with CHCl3. IIIa (10 g.) and Na malonate (from 2.8 g. Na and 28 ml. malonic ester), was mixed 1 hr., H2O added to dissolve the precipitate and the aqueous layer treated with 40% H2SO4 to pH 5 to give III [X = CH(CO2Et)2] (IIIc), m. 160-1° (alc.), (yield 11.7 g.). Similarly obtained was 95% III [X = CH(CO2Et)2] (IVc), m. 211-12°, IIIc (3 g.) was boiled 30 min. with 15 ml. 18% HCl to give 93% 1.6 g. III (X = Me), m. 213-14° (Me2CO). Similarly, IVc gave 95% IV (X = Me), m. 259-61°. To 1 g. IIIc in 15 ml. CHCl3 was added 0.25 ml. SO2Cl2 in 1 ml. CHCl3 and the mixture kept 12 hrs. to give 1 g. III [X = CCl(CO2Et)2], m. 139-40° (CCl4). Similarly, IVc gave 95% IV [X = CCl(CO2Et)2], m. 176-7°. To prepare III (X = NHMe), m. 359-60°, 1 g. IIIa was dissolved in 3 ml. 30% NH2Me. IIIa (4.4 g.) was heated at 40-50° with 1.35 g. KCN or 1.9 g. CuCN in 45 ml. HCONMe2 to give 3.1 g. III (X = CN), m. 194-5° (PhMe).
IT **24168-14-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 24168-14-7 CAPLUS
CN Xanthine, 3,7,8-trimethyl-2-thio- (8CI) (CA INDEX NAME)



L9 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:491430 CAPLUS Full-text

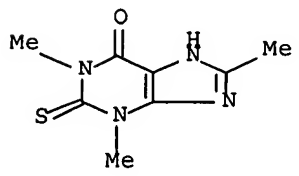
DOCUMENT NUMBER: 71:91430
TITLE: Chemistry of nucleophilic carbenes. XVI. 2-Thiocaffeine and 5-oxo-7-methylimino-1,4-dimethyl-1,4,5,7-tetrahydroimidazo[4,5-d][1,3]thiazine
AUTHOR(S): Walentowski, Ruediger; Wanzlick, Hans W.
CORPORATE SOURCE: Tech. Univ. Berlin, Berlin, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1969), 102(9), 3000-5
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB 1,3,7-Trimethylhypoxanthinium nitrate, prepared from 1-methyl-4-methylamino-5-(N-methylcarbamoyl)imidazole, was treated with S to give 2-thiocaffeine [5-thioxo-7-oxo-1,4,6-trimethyl-4,5,6,7-tetrahydroimidazo-[4,5- d]pyrimidine] (I). The "2-thiocaffeine" described by H. Biltz and H. Rakett (1928), was found to be 5-oxo-7-methylimino-1,4-dimethyl-4,5- dihydro-7H-imidazo[4,5-d]thiazine (II).
IT **24049-32-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 24049-32-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:496632 CAPLUS Full-text
DOCUMENT NUMBER: 69:96632
TITLE: Reactions of 4,5-diaminouracils with β-oxoesters
AUTHOR(S): Stahl, P. H.; Merz, K. W.
CORPORATE SOURCE: Univ. Freiburg/Br., Freiburg/Br., Fed. Rep. Ger.
SOURCE: Pharmazie (1967), 22(11), 630-4
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB 5,6-Diamino-1,3-dimethyluracil (I) refluxed with an equimol. amount of AcCH2CO2Et gave 80% II (X = Y = O, R = Me), decompose 216-19°; 2,4-dinitrophenylhydrazone m. 255-8°. Following II were prepared (X, Y, R, m.p., m.p. after resolidification, and m.p. of 2,4- dinitrophenylhydrazone given): O, O, Ph, 250-2°, 310-40°, 268-70°; O, O, 4-O2NC6H4, 259-63°, 360°, -; O, O, pyridin-3-yl, 260-3°, 245°, 261-2°; O, O, α-furyl, 224-32°, -, -; O, S, Me, 225-8°, -, -; S, S, Me, 212°, -, -; O, S, Ph, 223-9°, -, -; S, O, pyridin-3-yl, 257-63°, -, -; O, S, pyridin-3-yl, 244-53°, -, -; S, O, 4-O2NC6H4, 230-5°, 290-300°, -; O, S, 4-O2NC6H4, 240-2°, -, -; S, S, 4-O2NC6H4, 225°, -, -. 1,3-Dimethyl-4,5-diamino-2-thiouracil (3.7 g.) and 2.6 g. AcCH2CO2Et refluxed in

xylene 5 hrs. gave 86% 2,3,6,7,8,9-hexahydro-4,6,8-trimethyl-7- thio-2,9-dioxo-1H-pyrimido[4,5b] - 1,5-diazepine, m. 240-90°, which was converted into 1,3-dimethyl-4-amino-5-(acetoacetylamino)-2-thiouracil; 2,4-dinitrophenylhydrazone m. 245-7°. Also prepared was 1.3-dimethyl-4-amino-5-(1-ethoxycarbonyl-2-propylideneamino)-2-thiouracil, m. 210-22° (after resolidification m. 320-30°), which, heated to 250° and treated with NaOH gave 44% 8-methyl-2- thiotheophylline, m. 340-3°. I (2.55 g.) refluxed with 10 g. AcCH2CO2Et in 100 ml. PhNO2 gave 45.4% 8-methyltheophylline, m. 330°; picrate m. 282-305°.

IT **19673-55-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 19673-55-3 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,8-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)

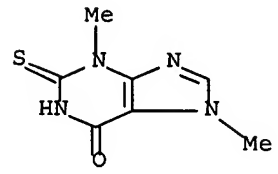


L9 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:427585 CAPLUS Full-text
DOCUMENT NUMBER: 69:27585
TITLE: Preparing theobromine derivatives substituted in the 2 position
INVENTOR(S): Golovchinskaya, E. S.; Nikolaeva, L. A.; Ovcharova, I. M.
PATENT ASSIGNEE(S): Ordzhonikidze, S., All-Union Scientific-Research Chemical-Pharmaceutical Institute
SOURCE: U.S.S.R. From: Izobret., Prom. Obraztsy, Tovarnye Znaki 1967 44(19), 36.
CODEN: URXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 202153		19670914	SU	19660727

ED Entered STN: 12 May 1984
AB The title compds. are prepared from the reaction of theobromine with POCl3 with boiling; the excess POCl3 is distilled from the reaction mass, the residue treated with a mixture of ice and NaHCO3 at a pH of 6-7 and the resulting 2-chlorotheobromine treated with nucleophilic reagents with boiling, e.g., with a 25% aqueous solution of NH3, thiourea, an alc. solution of Na alcoholate, or Na malonate, in PhMe.
IT **19373-97-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 19373-97-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



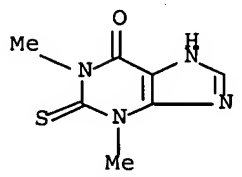
L9 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:420841 CAPLUS Full-text
DOCUMENT NUMBER: 65:20841
ORIGINAL REFERENCE NO.: 65:3877f-h,3878a-c
TITLE: Purine derivatives. III. Sulfur-containing theophyllines. I
AUTHOR(S): Merz, K. W.; Stahl, P. H.
CORPORATE SOURCE: Univ. Freiburg/Br., Germany
SOURCE: Beitr. Biochem. Physiol. Naturstoffen, Festschr. (1965) 285-98
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 22 Apr 2001
GI For diagram(s), see printed CA Issue.
AB cf. CA 63, 4296b. It is easy to prepare 6-thiotheophylline (I) by heating theophylline with P4S10 in a pyridine base b. 140-60° but 2,6-dithiotheophylline (II) can only be prepared (in very small quantities) from theophylline by melting it together with P4S10. 2-Thiotheophylline (III) was prepared first. Ethyl cyanoacetate, N,N'-dimethylthiourea, and NaOMe was refluxed 15 hrs. in a mol. ratio of 1.5:1:1.5 to give 34.5% 1,3-dimethyl-4-amino-2-thiouracil (IV), m. 289-90°. IV suspended in H2O and AcOH, or in HCONH2, was cooled in ice and NaNO2 added dropwise to give blue-green 1,3-dimethyl-4-amino-5-nitroso-2-thiouracil (V), m. 218-20°. V was reduced with Na dithionate at 100°, when 2-5 g. IV was used. When 10-30 g. IV was used, Na dithionate was used as starter, but the reduction itself was effected by formic acid. In both cases, 1,3-dimethyl-4,5-diamino-2-thiouracil (VI), m. 240-3°, was formed, and when HCONH2 was still present, 1,3-dimethyl-4-amino-5-formylamino-2- thiouracil (VII), m. 304-5°, was formed immediately. By heating VII for 0.5 hr., III, m. 344-8°, was formed, from which II, m. 267-9°, was prepared with P4S10 in pyridine with 1% H2O. It was not possible to prepare the nitroso compound from the orange 1,3dimethyl-4-amino- 2,6-dithiouracil (VIII), m. 273-5° (prepared from IV with P4S10), or from 1,3-dimethyl-4-amino-6-thiouracil (IX), m. 283-6° because of the lower electronegativity of the S, compound with the original O. By boiling 1,3-dimethyl-4,5-diaminouracil (X) or VI 12 hrs. with P4S10 in pyridine, 1,3-dimethyl-4,5-diamino-6-thiouracil (XI), and 1,3-dimethyl-4,5-diamino-2,6-dithiouracil (XII) were prepared, resp. With formamide the ring was closed and I, m. 311°, and II, were formed. From VI in stoichiometric ratio with HNO2 4,5,6,7-tetrahydro-4,6-dimethyl- 5-thio-7-oxo-v-triazolo[4,5-d]pyrimidine (XIII), m. 229°, was obtained; this was not possible with XI and XII. The S in III and I was substituted by 2H, by boiling the compound with Raney Ni in a dilute NH3 solution, to give 1,2,3,6-tetrahydro-1,3-dimethyl-6-oxopurine (XIV), and 1,2,3,6-tetrahydro-1,3-dimethyl-2-oxopurine (XV), resp., but neither of the S atoms could be substituted in the same way in II.

Identification was by thin-layer chromatography on silica gel with 80:12:5 C6H6-EtOHAcOH. In the uv spectra of the compds. a bathochromic shift of the absorption bands with regard to theophylline was observed. This increased in the order: III, I, II. Also the number of maximum increased, and in methanol solution the intensity of the strongest absorption bands increased in the same order. 21 references.

IT 6603-63-0, Theophylline, 2-thio-
(spectrum of)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:93480 CAPLUS Full-text

DOCUMENT NUMBER: 64:93480

ORIGINAL REFERENCE NO.: 64:17597b-h,17598a-e

TITLE: Syntheses in the purine series. XVII. Syntheses of N,S-purinium betaines

AUTHOR(S): Bredereck, Hellmut; Schellenberg, Peter; Nast, Roland; Heise, Hartmut; Christmann, Otto

CORPORATE SOURCE: Tech. Hochsch., Stuttgart, Germany

SOURCE: Chemische Berichte (1966), 99(3), 944-57
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 64:93480

ED Entered STN: 22 Apr 2001

GI For diagram(s), see printed CA Issue.

AB cf. CA 57, 15107e. 7,9-Dimethyl- and 1,7,9-trimethyl-N,S-purinium betaines were prepared by the conversion of OH, SH, or PhCH2S groups in 7,9-dimethyl- and 1,7,9-trimethylpurinium salts, resp., into the SH group and subsequent liberation from the resulting salts. Hypoxanthine (1.5 g.) in 15 g. p-MeC6H4-SO3Me (I) stirred 15 min. at 250° and diluted with 25 cc. BuOH and then 150 cc. Et2O yielded 2.3 g. 6-hydroxy-7,9- dimethylpurinium p-toluenesulfonate (II), m. 255-6° (BuOH). II (3.36 g.) and 80 cc. POCl3 refluxed 2 hrs. and evaporated, treated with 125 cc. absolute EtOH and 7 g. CS(NH2)2 (III), refluxed 2 hrs., cooled, diluted with 400 cc. MeOH, and saturated with dry NH3 yielded 1.14 g. pale yellow IV (R = H) (V), m. 283° (decomposition from 265° with sintering). 2-NH2 derivative (3 g.) of II and 150 cc. POCl3 refluxed 4 hrs., evaporated, treated with 200 cc. absolute EtOH and 10 g. III, refluxed 3.5 hrs., and saturated at 30-5° with dry NH3 yielded 0.375 g. IV (R = NH2) (VI), m. 312° (decomposition) with sintering from 295°. 2-MeS derivative (1.91 g.) of II and 60 cc. POCl3, 60 cc. EtOH, and 5 g. III yielded similarly 0.81 g. IV (R = MeS) (VII), m. 277° (decomposition) with sintering from 265°. 7,9-Dimethylxanthinium p-toluenesulfonate (VIII), 125 cc. POCl3, and 0.38 cc. H2O refluxed 3.5 hrs. and then treated with 150 cc. absolute EtOH and 10 g. III followed by NH3 gave 1.32 g. pale yellow IX (R = H) (X), m. 300°

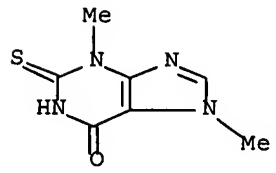
(decomposition) with sintering from 285°. 1-Me derivative (3.66 g.) of VIII gave similarly 0.64 g. XI (R = Me) (XII), m. 248° (MeOH). 2-Amino-6-mercaptopurine (0.5 g.) and 5 g. I stirred 10 min. at 117°, diluted with an equal volume EtOH, and treated dropwise with dry Et2O gave 0.86 g. VII, m. 281°. VII (2.5 g.) added in portions with stirring to Cl in absolute MeOH gave 0.75 g. 2-amino-6-chloro-7,9-dimethylpurinium chloride (XIII), m. 293° (EtOH); picrate, m. 209° (EtOH). XIII (0.5 g.), 80 cc. absolute EtOH, and 0.5 g. III refluxed 4 hrs. yielded 0.32 g. pale yellow-green 6-SH analog (XIV) of XIII, m. 275°. XIV in MeOH treated with dry NH3 gave VI. 6-Hydroxy-2-thioxodihydropurine (1.68 g.) in 0.4 g. NaOH in 50 cc. H2O treated dropwise with stirring at room temperature during 1 hr. with 1.61 g. PhCH2-Cl in 20 cc. MeOH and stirred 4 hrs. yielded 1.6 g. 6-hydroxy-2-benzylthiopurine (XV), m. 262-3° (absolute EtOH). XV (0.5 g.) and 5 g. I yielded 0.69 g. 6-hydroxy-2-benzylthio-7,9-dimethylpurinium p-toluenesulfonate (XVI), m. 240° (EtOH). 2,6- Dithioxotetrahydropurine (2.3 g.) in 250 cc. H2O and 1.6 g. NaOH treated dropwise during 2 hrs. with 4.6 g. PhCH2Br in 20 cc. MeOH and stirred 5 hrs. yielded 3.1 g. 2,6-bis(benzylthio)purine (XVII), m. 196° (absolute EtOH). XVII (2.5 g.) and 20 g. I stirred 10 min. at 170° yielded 2.02 g. 2,6-bis(benzylthio)7,9-dimethylpurinium p-toluenesulfonate (XVIII), m. 170° (absolute EtOH). 2-Benzylthio-6-thioxo-1- methyldihydropurine (3 g.) and 20 g. I stirred 1 hr. at 150°, cooled, and diluted with 20 cc. absolute EtOH and 500 cc. Et2O, and the oily precipitate treated in 500 cc. boiling H2O with 10 cc. 65% HClO4 yielded 2.4 g. 2-benzylthio-6-thioxo-1,7,9-trimethyldihydropurinium perchlorate (XIX), m. 177° (absolute EtOH). 2-Amino-6-benzythiopurine (0.5 g.) and 5 g. I gave similarly after treatment of the product with 65% HClO4 0.56 g. 2-amino-6-benzylthio-7,9-dimethylpurinium perchlorate (XX), m. 226° (EtOH). XVI (0.5 g.), 2 g. AlBr3, and 60 cc. dry MePh stirred 6 hrs. at 80° gave 0.16 g. XI (R = H) (XXI), m. 297° (H2O). XVIII (1 g.), 4.0 g. AlBr3, and 100 cc. dry MePh gave similarly 0.34 g. (crude) pale yellow XXII (R = H) (XXIII), m. 283° (decomposition) (H2O). XIX (1 g.), 5 g. AlBr3, and 150 cc. dry MePh yielded similarly 0.245 g. (crude) yellow XXII (R = Me) (XXIV), m. 255° (decomposition). XX (0.5 g.), 2 g. AlBr3, and 60 cc. dry MePh gave 0.24 g. pale yellow 2-amino-6-mercapto-7,9- dimethylpurinium bromide, m. 270° (EtOH); a 0.5-g. portion in 25 cc. MeOH treated with dry NH3 gave 0.31 g. VI, m. 312°. 6-Oxo-2-thioxo-3-methyltetrahydropurine (4.0 g.) in 250 cc. H2O and 2.0 g. NaOH with 4.1 g. PhCH2Br yielded 4.6 g. 2-benzylthio-6-oxo-3-methyldihydropurine (XXV), m. 218° (absolute EtOH). XXV (1.0 g.) and 5.0 g. I stirred 45 min. at 150°, and the oily product treated in 100 cc. BuOH with 3 cc. 65% HClO4 and then 200 cc. Et2O yielded 0.56 g. 2-benzylthio-6-oxo-3,7,9-trimethyldihydropurinium perchlorate (XXVI), m. 202° (absolute EtOH). XXVI (1.0 g.), 5.0 g. AlBr3, and 150 cc. dry MePh yielded 0.45 g. (crude) 6-oxo-2-thioxo-3,7-dimethyltetrahydropurine, m. 308° (with sintering from 290°) (H2O). V (0.200 g.) added in portions to 1 cc. 30% H2O2, and the sirupy product in 20 cc. MeOH treated successively with 0.5 cc. 30% H2O2 and dry NH3 gave 0.115 g. 6-hydroxy-7,9-dimethylpurinium betaine (XXVII). Hypoxanthine (1.5 g.) in 15.0 g. I stirred 15 min. at 150° gave 2.3 g. 6-hydroxy-7,9- dimethylpurinium p-toluenesulfonate (XXVIII), m. 255-6° (BuOH). XXVIII (1.5 g.) in 150 cc. hot MeOH treated at room temperature with dry NH3 gave 0.5 g. XXVII, m. 309°. XXVII (about 100 mg.) in 10-20 cc. MeOH treated with 5-6 drops 65% HClO4 gave the perchlorate analog of XXVIII, m. 171° with sintering from 130° (BuOH). X.H2O (0.400 g.) added in portions at 30° to 2 cc. 30% H2O2 and treated after 2 hrs. with dry NH3 yielded 0.175 g. 7,9-dimethylxanthinium betaine (XXIX) (perchlorate, m. 281°), which was also obtained similarly from VII, XXI, and XXIII. 2-Hydroxy-6-thioxo1-methyldihydropurine (3.64 g.) and 6.0 g. I in 25 cc. AcNMe2 heated 15 min. at 145° gave 4.13 g. (crude) 2-hydroxy-6-thioxo-1,7,9-trimethyldihydropurinium p-toluenesulfonate; a 3.00-g. portion in 150 cc. MeOH treated at room temperature with concentrated NH4OH yielded 0.85 g. 2-hydroxy-6-thioxo-1,7,9- trimethyldihydropurinium betaine (XXX), m. 355-7° (decomposition) (H2O). The oxidation of XXX with H2O2 gave 1,7,9-trimethylxanthinium betaine (XXXa) which was also obtained from XII and XXIV.

VI oxidized similarly gave 2-amino-6-hydroxy-7,9-dimethylpurinium betaine (XXXI). The Rf values were determined with 2:1 BuOH-5N AcOH (A), 2:1 PrOH-H2O (B), 5% aqueous NH4Cl (C), and 4% aqueous Na citrate (D), and the pKa, values in H2O at 20° were measured potentiometrically or spectroscopically for the compds. listed in the table. The uv spectra of X, XII, XXI, XXIII, XXIV,XXX are recorded.Compound, A, B, C, D, pKa; V, 0.40, 0.60, 0.81, 0.80, 5.56 ± 0.04; VI, 0.41, 0.51, 0.66, 0.71, 6.28 ± 0.03; VII, 0.62, 0.75, 0.74, 0.66, 4.74 ± 0.08; X, 0.32, 0.50, 0.70, 0.65, 1.9 ± 0.2; XXX, 0.58, 0.72, 0.69, 0.66, 2.1 ± 0.2; XXI, 0.25, 0.41, 0.77, 0.73, 1.85 ± 0.2; XII, 0.42, 0.63, 0.79, 0.76, 1.95 ± 0.2; XXIII, 0.38, 0.57, 0.63, 0.58, 0.83 ± 0.13; XXIV, 0.57, 0.75, 0.57, 0.55, 0.71 ± 0.04; XXVII, 0.28, 0.50, 0.58, 0.87, --; XXXI, 0.30, 0.46, 0.81, 0.84, --; XXIX, 0.21, 0.38, 0.85, 0.76, --; XXXa, 0.40, 0.58, 0.90, 0.84, --; .

IT **19373-97-8P**, Theobromine, 2-thio-
RL: PREP (Preparation)
(preparation of)

RN 19373-97-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:84708 CAPLUS Full-text
DOCUMENT NUMBER: 60:84708
ORIGINAL REFERENCE NO.: 60:14874c-e
TITLE: Action of 8-azaguanine and 8-azaxanthine on Pseudomonas aeruginosa
AUTHOR(S): Bergmann, F.; Ungar-Waron, Hanna; Kwietny-Govrin, Hanna
CORPORATE SOURCE: Hebrew Univ.-Hadassah Med. School
SOURCE: (1964), 91(2), 270-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001

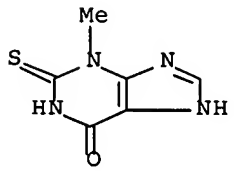
AB 8-Azaguanine does not inhibit the growth of P. aeruginosa, but undergoes slow deamination. 8-Azaxanthine arrests the growth of this species temporarily. This growth retardation is abolished by hypoxanthine, xanthine, and a number of unnatural purines. During growth inhibition by azaxanthine, the xanthine oxidase-like activity of the bacterial cells is enhanced. Much larger increments of enzymic activity are obtained by the addition of hypoxanthine, xanthine, or certain unnatural purines, which all contain an unsubstituted imidazole ring. During growth inhibition by 8-azaxanthine, the urate oxidase-like activity of the bacteria is strongly depressed. On the other hand, the addition of hypoxanthine or xanthine to the culture medium produces a huge increase in the enzymic activity of the normal strain. After the 1st exposure to 8-azaxanthine a resistant strain emerges. This strain shows normal xanthine oxidase and urate oxidase activities, even when growing in the presence of the antimetabolite. Benzimidazole and benzotriazole are weak

growth inhibitors. They depress xanthine oxidase activity of the bacterial cells, but leave their urate oxidase activity unaffected.

IT 28139-02-8, Xanthine, 3-methyl-2-thio-
(effect on Pseudomonas aeruginosa response to 8-azaxanthine)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1963:60954 CAPLUS Full-text

DOCUMENT NUMBER: 58:60954

ORIGINAL REFERENCE NO.: 58:10464a-e

TITLE: Relation of structure to the inhibitory activity of purines against urate oxidases

AUTHOR(S): Bergmann, F.; Kwietny-Govrin, Hanna; Ungar-Waron, Hanna; Kalmus, A.; Tamari, M.

CORPORATE SOURCE: Hebrew Univ.-Hadassah Med. School, Jerusalem

SOURCE: Biochemical Journal (1963), 86, 567-74
CODEN: BIJOAK; ISSN: 0264-6021

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

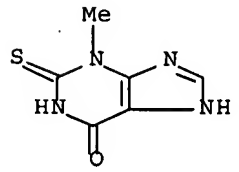
AB cf. ibid. 292. The inhibitory activity of a variety of compds. against urate oxidase has been determined: I50 values in μM were for hypoxanthine 220, 8-hydroxy-purine 110, 2-hydroxypurine 12, 2,8-dihydroxypurine 5.2, xanthine 18, 6,8-dihydroxypurine 66, 6-mercaptopurine 700, 6-thioxanthine 2.7, 2-thioxanthine 190, 8-hydroxy-6-mercaptopurine 70, 6-hydroxy-8-mercaptopurine 500, 6,8-dimercaptopurine 370, 8-hydroxy-2-mercaptopurine 500, 2-hydroxy-8-mercaptopurine 12, 2-thiouric acid 250, 6-thiouric acid 14, 8-thiouric acid 5, 2,6-dithiouric acid 150, 2,8-dithiouric acid 80, 6,8-dithiouric acid 0.4, 6,8-dihydroxy2- methylmercaptopurine 500, 2,6-dihydroxy-8-methylmercaptopurine 38, 2-hydroxy-6-methylmercaptopurine 6, 8-hydroxy-6methylmercaptopurine 32, 2,8-dihydroxy-6-methylmercaptopurine 0.1,3, 8-hydroxy-3-methyl-6- methylmercapto-2-oxopurine 7, 4,5-diamino-6-thiouracil 38, 2,4-dihydroxypteridine 300, 2,4,6trihydroxypteridine 150, 2,4;6,7-tetrahydroxypteridine 500, 8-aza-6-hydroxypurine 47, 8-aza-2-hydroxypurine 1.6, 8-azaxanthine 5.9, 3-methyl-2-thiouric acid 150, 3-methyl-6-thiouric acid 400, 3-methyl-8-thiouric acid 190, 3-methyl-2-thioxanthine 100, 3-methyl-6-thioxanthine 100, 7-methyl-6-thioxanthine 1000. The inhibitory effect was used to measure the affinity of the inhibitors for the enzyme. Of the 3 O atoms of uric acid, that of the 2-carbonyl group possesses the greatest binding power for the active center. Replacement of this O atom by S greatly diminishes the inhibitory activity. Combination of a 2-carbonyl group with S at C-6 enhances inhibitory activity considerably. On certain purine derivs., a 6-methylmercapto substituent is more effective than a 6-thiocarbonyl group. 2,6-Dihydroxy-6methylmercaptopurine is the most potent inhibitor of urate oxidase known so far. Replacement of the imidazole moiety of the purine ring by triazole

enhances affinity, whereas introduction of the pyrazine ring, as in pteridines, greatly decreases it. Free imino groups are essential for the attachment of purines to urate oxidase, as N-methylation weakens or abolishes the inhibitory effect. On the other hand, in 2-thiopurines, methylation at N-3 increases the inhibitory power.

IT **28139-02-8**, Xanthine, 3-methyl-2-thio-
(uric oxidase inhibition by)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 34 OF 47 CAPLUS . COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:436343 CAPLUS Full-text

DOCUMENT NUMBER: 57:36343

ORIGINAL REFERENCE NO.: 57:7262i,7263a-e

TITLE: Preparation and properties of 1,2-dihydrophthalazine derivatives

AUTHOR(S): Smith, Richard F.; Otremba, Edward D.

CORPORATE SOURCE: State Univ. Coll., Albany, NY

SOURCE: Journal of Organic Chemistry (1962), 27, 879-82
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:36343

ED Entered STN: 22 Apr 2001

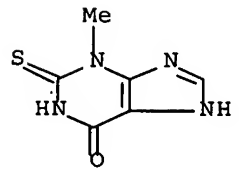
AB cf. CA 53:17143d. Reduction of 2-methyl-and 2-ethylphthalazinium iodide (I, II) with aqueous NaBH4 yielded the corresponding 2-alkyl-1,2-dihydrophthalazines (III, IV). H2O (3 l.) containing 0.3 mole o-HO2CC2H4CHO stirred at 80° with 0.3 mole (N2H4)2.H2SO4 and 1 1.1 .0N NaOH, the green suspension evaporated in vacuo to 200 ml., extracted with C6H6, and the dried (MgSO4) exts. evapd, yielded 50% phthalazine (V), m. 87-90°. Further extraction of the aqueous solution with EtOAc gave 0.9 g. 1(2H)-phthalazinone, m. 183-4°. I, m. 240-3° (decomposition), heated with saturated alc. picric acid (20 ml./g, halide) gave 75% picrate, m. 199-200° (decomposition). II, m. 225-8° (decomposition) (alc.), similarly yielded 93% II picrate, m. 167-9°. V (2 g.) and 4 ml. PhCH2Cl refluxed 3 hrs. in 15 ml. dry MeOH, the cooled mixture diluted with anhydrous Et2O, kept overnight, and the Et2O-washed product dried in vacuo yielded 89% extremely hygroscopic 2-benzylphthalazinium chloride (VI), m. 175-8° (alc.-Et2O); picrate m. 183-4° (MeOH). The powdered quaternary salts added portionwise to 3% aqueous NaBH4 (3:1 salt-hydride), the cooled mixture extracted with Et2O, the extract dried (MgSO4), and the product isolated gave 2-alkyl-1,2-di-hydrophthalazines. Distillation yielded 75% III, b17 129-30°; HCl salt m. 133-5° (decomposition) (alc.); pierate m. 95-8° (decomposition); MeI salt (VII) m. 173-6° (MeOH). III on exposure to air rapidly yielded 2-methyl-1(2H)-phthalazi-none, m. 108-10°. IV HCl salt, m. 142-4° (decomposition) (alc.), converted to the free base, refluxed 6 hrs. with excess MeI in ale., the resultant highly deeompd, tarry product extracted

with EtOAc and the extract diluted with Et2O gave IV MeI salt, m. 155-7° (alc.). VI (4.0 g.) reduced with aqueous NaBH4, the oily product refluxed 3 hrs. with 7 ml. MeI in 25 ml. alc., and the mixture cooled gave 1.4 g. VII. Dilution of the filtrate c with Et2O gave 1.4 g. unidentified material, m. 138-42°, recrystd. from alc.-Et2O to give a sample, m. 140-2° (decomposition), melting with evolution of a potent lacrimator. VII (1 g.) in 10 ml. H2O treated with 10 ml. 6N NaOH and the oily product extracted with Et2O gve o-Me2NCH2C4CN; picrate m. 144-5°; MeI salt m. 184-5°; HCl salt m. 226-7° (alc), v 2220 cm.-1, identical with the salt prepd, by stirring 0.05 mole each o-BrCH2C6H4CN, Me2NH.HCl, and anhydrous Na2CO3 2 days at 20° in 50 ml. MeOH, acidifying the coned, solution with dilute HCl, basifying the Et2O-washed aqueous layer, extracting with Et2O, and treating the dried extract with anhydrous HCl.

IT **28139-02-8P**, Xanthine, 3-methyl-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:436342 CAPLUS Full-text

DOCUMENT NUMBER: 57:36342

ORIGINAL REFERENCE NO.: 57:7262h-i

TITLE: Condensed pyrimidine systems. XXII. N-methyl purines

AUTHOR(S): Elion, Gertrude B.

CORPORATE SOURCE: Burroughs Wellcome and Co. Inc., Tuckahoe, NY

SOURCE: Journal of Organic Chemistry (1962), 27, 2478-91
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:36342

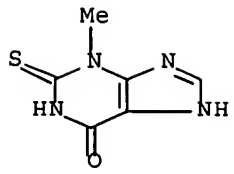
ED Entered STN: 22 Apr 2001

AB cf. CA 54, 18531b. A group of 1-and 3-monomethylpurines has been prepared by complete synthesis. Among the new derivs. are 3-methyladenine, 3-methylguanine, and the 1-and 3-methyl derivatives of 6-mercaptopurine. A number of 7- and 9-methyl derivs. have been obtained by direct methylation of 6-chloropurine, conversion to the mercapto derivs., and subsequent separation of the 7- and 9-methylpurine-6-thiols. Several ring openings and rearrangements have been observed in the course of attempts to prepare 1-methyladenine.

IT **28139-02-8P**, Xanthine, 3-methyl-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



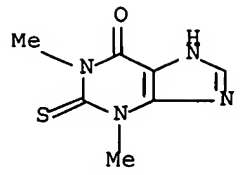
L9 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:429662 CAPLUS Full-text
DOCUMENT NUMBER: 57:29662
ORIGINAL REFERENCE NO.: 57:5924h-i,5925a-i,5926a-b
TITLE: The synthesis of some 6-thioxanthines
AUTHOR(S): Wooldridge, K. R. H.; Slack, R.
CORPORATE SOURCE: May Baker Ltd., Dagenham, UK
SOURCE: Journal of the Chemical Society (1962) 1863-28
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 57:29662
ED Entered STN: 22 Apr 2001
AB A series of 1,3- and 3,7-disubstituted 6-thioxanthines, of interest as broncho and coronary dilators, has been prepared by the selective thionation of the corresponding xanthines with P2S5 in C5H5N. 1,3,7-Trialkyl-6- thioxanthines could not be prepared in this way but were readily obtained front 1,3-dialkyl-6-thioxanthines. Theophylline (50 g.), 100 g. P2S3, and 1. dry C5H5N refluxed 8 hrs. with stirring, cooled, diluted with stirring during 1 hr. with 2 l. H2O, concentrated to about 1/3 volume, cooled, and filtered, and the residue dissolved in 2N NaOH, filtered, and repptd. with dilute HCl yielded 51 g. 1,3-dimethyl-6-thioxanthine (I), pale yellow needles, m. 323-5° (decomposition) (EtOH or H2O). 6-Thiotheobromine (75 g.) with 150 g. P2S5 gave similarly 72 g. 3,7-dimethyl-6-thioxanthine (II), m. 300-1°. (MeNH)2CS (79 g.) added in portions with stirring during 0.5 hr. to 65 g. NCCH2CO2H in 156 g. Ac2O and 200 cc. AcOH at 65°, kept 2 hrs. at 65% evaporated at 69-5° in vacuo, and the gummy residue stirred at 50° with 200 cc. H2O and adjusted to pH 10 with 50% aqueous NaOH gave 65 g. 6-amino-1,3-dimethyl 2-thiouracil (III), prisms, m. 286-8° (EtOH). The crude III suspended in 6000 cc. H2O containing 25.5 g. NaNO2 at 80-90 °, 50 cc. AcOH added during 15 min., and the mixture stirred 15 min. at 80-90° and cooled yielded crude 5-NO derivative (IV) of III, blue-green amorphous solid, m. 215-16° (decomposition). The IV added in 5-g. portions to 2.5 l. H2O at 70-80° together with sufficient Na2S2O4 to discharge the color of the IV, cooled, and filtered, the residual 5-NH2 derivative of III, m. 230-4°, added immediately to 500 cc. 2N H2SO4, the resulting sulfate (57 g.) boiled 0.5 hr. with 500 cc. HCONH2, diluted with 250 cc. H2O, and cooled, and the yellow solid dissolved in 300 cc. hot 17% NH4OH, filtered, and acidified to pH 4 with AcOH yielded 47 g. 1,3dimethyl-2-thioxanthine, m. 344-8°. Me2SO4 (25.2 g.) added dropwise in 15 min. with stirring at 40° to 35 g. I and 100 cc. 2N NaOH, kept 0.5 hr. at 40°, cooled, and filtered gave 15 g. 1,3,7-trimethyl-6-thioxanthine (V), pale yellow prisms, m. 246-7°. II (17.5 g.) and 42.5 g. Me2SO4 gave 1 g. V, m. 247-9°. II(10g.)in 125 cc. 0.5N NaOH stirred 2 hrs. at room temperature with 10.7 g. MeI yielded 6.7 g. 1,2,3,4tetrahydro-3,7-dimethyl- 1-methylthiopurine, needles, m. 300-3° (H2O). The appropriate urea was converted by the method of Traube [Ber. 33, 3035(1900)] or of Speer and Raymond (CA 48, 1346h) or of Montgomery (CA 50,

13932b) to the corresponding 1,3-dialkylxanthines (1- and 3-alkyl group and m.p. given): Me, MeO(CH2)3, 166-8°; Me, furfuryl, 255-8°; Et, iso-Bu, 195-7°; Pr, iso-Bu, 189-92°; Bu, Me, 207-10°. Similarly were prepared 3-isobutylxanthine (VI), m. 299-301°, and the 7-Me derivative of VII, m. 239-41°. P2S5 (600 g.) and 482 g. 3-isobutyl-1-methylxanthine in 4.2 l. dry C5H5N, refluxed 9 hrs. with stirring, cooled to about 40°, diluted carefully with H2O, concentrated to about 2.5 l., diluted with 3.5 l. H2O, and filtered, and the residue dissolved in 2.5 l. warm N NaOH, filtered, and acidified with concentrated HCl to pH 4 pp.d. 426 g. 3-isobutyl-1-methyl-6-thioxanthine (VII), yellow prisms, m. 170-2° (EtOH). Similarly were prepared the following 1,3-disubstituted-6-thioxanthines (1- and 3-substituent, m.p., and % yield given): Me, Me (VIII), 3235°, 94; Me, Et, 235-7°, 79; Me, Pr, 164-7°, 63; Me, Bu, 156-8°, 73; Me, Am, 169-70°, 50; Me, C6H13, 167-74°, 78; Me, iso-Am, 156-60°, 50; Me, MeO(CH2)3, 150-2°, 50; Me, CH2:CHCH2, 152-6°, 81; Me, CH:CMeCH2, 195-8°, 47; Me, PhCH2, 213-15°, 84; Me, Ph(CH2)2, 198-9°, 63; Me, furfuryl, 184-6°, 15; Et, Me, 235-9°, 76; Et, Et, 2568°, 72; Et, Bu, 175-8°, 74; Et, iso-Bu, 180-3°, 39; Et, CH2:CHCH2, 210-12°, 49; Pr, Pr, 212-15°, 89; Bu, Me, 295-8°, 84; Bu, Bu, 183-6°, 72. Similarly were prepared the following 8-substituted VIII (substituent, m.p., and % yield given): Me, 294-5°, 75; Et, 218-19°, 76; SH, 240° (decomposition), 83. I (42 g.) and 8.6 g. NaOH in 150 cc. H2O stirred 0.5 hr. at room temperature, cooled, and filtered, and the dried Na salt (44 g.) of I dissolved in 200 cc. HCONMe2, treated with stirring during 15 min. at room temperature with 18.6 g. AcCH2Cl, stirred 0.5 hr., diluted with 300 cc. iced H2O, and filtered gave 21.3 g. 7-AcCH2 derivative (IX) of I, yellow needles, m. 208-10°. IX (21 g.), 269 g. paraformaldehyde, 11.9 g. piperidine-HCl, 1.6 cc. Et2O.BF3, and 200 cc. dry dioxane stirred 7 hrs. at 100° and filtered gave 23.0 g. 1,3-dimethyl-7(2-oxo-4-piperidinobutyl)-6-thioxanthine-HCl, yellow-brown prisms, m. 197-200°. In the same manner as VII were prepared the following 1,3,7-trisubstituted-6-thioxanthines (1-, 3-, and 7-substituents and m.p. given): Me, Me, Et, 22830°; Me, Me, Et2N(CH2)2, 52-4°; Me, iso-Bu, Et2N(CH2)2 [isolated as the (-)-di(p-toluoyl) D-tartrate], 120° (decomposition); Me, iso-Bu, AcCH2, 170-4°; Bu, Me, Me, 118-19°. in the same manner were prepared the following 3,7-dialkyl-6thioxanthines (3- and 7-substituents and m.p. given): Me, Me, 300-1°; Bu, Me, 200-3°; iso-Bu, Me, 228-30°. Also prepared was 3-methyl-6-thioxanthine, m. 269-74°. Choline chloride (3.4 g.) in 900 cc. hot iso-PrOH treated with stirring with 150 g. 85% KOH in 600 cc. absolute MeOH, cooled to 0°, filtered, treated with 500 g. VII, warmed a few min., and evaporated in vacuo, the residual sirup dissolved in 1 l. hot isoPrOH, treated with C, filtered, diluted with 1 l. dry Et2O, and cooled, and the precipitated filtered off gave 548 g. choline salt of VII, pale yellow prisms, m. 145-9°; their mother liquor evaporated, and the sirupy residue dissolved in H2O and acidified to pH 4 with HCl gave 8 g. VII. Similarly were prepared the choline salts of the following 1,3-disubstituted-6-thioxan-thines (1- and 3-substituents, m.p. and % yield given): Me, Me (X), 145-7°, 47; Me, Et, 157-9°, 72; Me, Pr, 145-50°, 72; Me, Bu, 133-5°, 88; Me, Am, 150-3°, 93; Me, C6H13, 55-7°, 94; Me, iso-Bu, 148.5-9.5°, 92; Me, iso-Am, 125-8°, 90; Me, CH2:CHCH2, 172-5°, 73; Me, CH2:CMeCH2, 145-51°, 80; Me, PhCH2, 166-71°, 80; Me, Ph(CH2)2, 173-5°, 80; Et, Me, 157-8°, 70; Et, Et, 142-7°, 92; Et, Bu, 115-18°, 79; Pr, Pr, 114-18°, 57; Bu, Me, 105-9°, 62. Also prepared were 8-Me derivative of X, 175-6°, 65, and the 8-SH derivative of X, 209 11°, 70. The ultraviolet absorption maximum of a number of thioxanthines are tabulated.

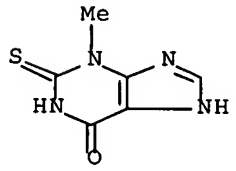
IT **6603-63-0P**, Theophylline, 2-thio-
RL: PREP (Preparation)
(preparation of)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:418827 CAPLUS Full-text
DOCUMENT NUMBER: 57:18827
ORIGINAL REFERENCE NO.: 57:3862h-i,3863a
TITLE: Specific reactions of the purine-oxidizlng system of Pseudomonas aeruginosa
AUTHOR(S): Bergmann, Felix; UngarWaron, Hanna; Kwietny-Govrin, Hanna; Goldberg, Hilda; Leon, Shalom
CORPORATE SOURCE: Hebrew Univ., Jerusalem, Israel
SOURCE: Biochimica et Biophysica Acta, Specialized Section on Nucleic Acids and Related Subjects (1962), 55, 512-22
CODEN: BBASB7; ISSN: 0926-6550
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Apr 2001
AB cf. CA 55, 26059g. Resting cells of -P. aeruginosa oxidized 2-aminopurine and its MeNH- and Me2N- analogs at C-8 in contrast to the action of mammalian xanthine oxidase. 6-Mercaptopurine was attacked 1st at C-2, then at C-8, and then further. This compound did not inhibit growing P. aeruginosa, but increased production of xanthine oxidase. The 3-Me derivs. of thioxanthines were oxidized at C-8, while 3methylhypoxanthine was first attacked at C-2. The resulting complex, containing 3-methylxanthine, dissociated before further oxidation to 3-methyluric acid, in contrast to xanthine. The results are discussed in reference to the mechanism of attack and the different actions of bacterial and mammalian xanthine oxidases. 21 references.
IT **28139-02-8**, Xanthine, 3-methyl-2-thio-
(oxidation by xanthine oxidase of Pseudomonas aeruginosa)
RN 28139-02-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:410979 CAPLUS Full-text
DOCUMENT NUMBER: 57:10979
ORIGINAL REFERENCE NO.: 57:2268g-i,2269a-i,2270a-c
TITLE: Alkaloids of Tylophora crebriflora-structure and

synthesis of tylocrebrine, a new phenanthroindolizidine alkaloid

AUTHOR(S): Gellert, E.; Govindachari, T. R.; Lakshmikantham, M. V.; Ragade, I. S.; Rudzats, R.; Viswanathan, N.

CORPORATE SOURCE: Univ. N. S. W., Sydney

SOURCE: Journal of the Chemical Society (1962) 1008-14
CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

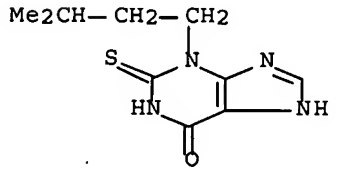
AB Milled T. crebrifiora (21 lb.) extracted with hot MeOH, the extract concentrated to small volume (4 l.), diluted with 2 l. H2O, concd, to 800 ml. in a climbing film evaporator, and the mixture filtered while warm gave a solid (I) and a filtrate (II). II acidified with dilute AcOH, extracted exhaustively with CCl4, the combined CCl4 solns, extracted with 2N HCl, the extract combined with the previous acidic phase, and filtered gave a filtrate (III), which gave a strong Mayer test and showed 2 fluorescent spots when chromatographed on paper in BuOH-AcOH (Rf 0.2 and 0.5). I in warm 2N AcOH diluted with hot H2O, cooled, filtered, the filtrate extracted with CCl4, combined with III, made basic with concd, aqueous, the precipitate (45 g.) repeatedly precipitated from hot aqueous AcOH with concd, aqueous NH3, extracted (Soxhlet) with MeOH, and the product crystd, from MeOH gave crude alkaloid mixture (IV). Crude IV (in 2 g. batches) subjected to partition chromatography in 15:85 PrOH-2N-AcOH on a cellulose column (partial separation into fractions with Rf 0.2 and 0.5), the fractions from several such chromatograms combined (intermediate fractions were rechromatographed), the 1st fraction evaporated in vacuo, the residue dissolved in warm dilute AcOH, made alkaline with concd, aqueous NH3 and the crude alkaloid [Rf 0.5 (in 3:97 AcOH-BuOH saturated with H2O) (solvent A)] crystallized 3 times from MeOH gave tylocrebrine (V), m. 218-20° (decomposition), λ 263, 342, and 360 mμ (ε 4.81, 3.25, and 3.09), [α]24D -45 ± 2° (c 0.74, CHCl3), pKa 6.7 (in 50% aqueous EtOH) [HI salt m. 214-17° (decomposition) (aqueous MeOH); perchlorate m. 262-4° (decomposition); picrate m. 134-6° (Me2CO containing a little MeOH)]. The crude alkaloid [Rf 0.2 (solvent A)] from the 2nd fraction recrystd. 3 times from CHCl3-MeOH gave tylophorine (isomeric with V), m. 282-4° (decomposition), λ 257, 290, 340, 355 mμ (ε 4.82, 4.51, 3.43, 2.96). V refluxed on a H2O bath with excess MeI in MeOH until dissolved, then refluxed 30 min. more, concentrated, and cooled gave optically active V.MeI, m. 255-8° (decomposition) (MeOH), [α]21D -30 ± 2° (c 0.30, MeOH). Optically active V.MeI refluxed 30 min. in 20% aqueous NaOH gave (±)-V.MeI, m. 264-6° (decomposition) (MeOH), [α]21D 0° (c 0.10, MeOH). V.MeI (1.4 g.) refluxed with AgCl in aqueous MeOH, the resulting V.MeCl shaken with Ag2O in H2O, the solution of V.MeOH evaporated to dryness, the residue heated 3 min. at 240°/0.2 mm., and the product chromatographed in C6H6 on basic Al2O3 gave 400 mg. VI, m. 144.5-5.0° (C6H6-petr. ether, then petr. ether). V.MeI (100 mg.) converted directly into V.MeOH (with Ag2O in 10 ml. H2O; 5 hr.), the mixture filtered, the filtrate evaporated in vacuo at 50° the residue heated 30 min. at 100°/0.05 mm., the product repeatedly extracted with hot C6H6, and chromatographed in C6H6 on Al2O3 gave 10 mg. VI, m. 144.5-5.0°. VI (50 mg.) in 3 ml. AcOH heated 5 min. at 125° with excess HIO4 gave no CH2O (no precipitate with dimedon). Et 3,4,6,7-tetramethoxyphenanthrene-9-carboxylate (3 g.) in 25 ml. dry tetrahydrofuran added to 1.5 g. LiAlH4 in 15 ml. tetrahydrofuran with stirring, stirred 4 hrs., treated with Et2O and H2O, the organic layer decanted, and evaporated gave 2.2 g. 9 - hydroxymethyl - 3,4,6,7 - tetramethoxyphenanthrene (VII), m. 164-5° (C6H6). VII (5 g.), 4 ml. SOCl2, and 0.5 ml. pyrldine in 120 ml. CHCl3 heated 15 min. at 40-60°, cooled, poured into H2O, extracted with CHCl3, the extract dried, concentrated to small volume, and diluted with petr. ether gave 4.2 g. 9-chloromethyl-3,4,6,7-tetramethoxyphenanthrene (VIII), m. 148° (decomposition) (C6H6-petr. ether).

VIII (4 g.) in 40 ml. dry tetrahydrofuran added dropwise with stirring to pyrrylmagnesium bromide (from 1.8 g. Mg, 5.8 ml. EtBr, and 5.26 ml. freshly distilled pyrrole) in Et2O cooled in ice under N, stirred 3 hrs. during which the mixture was allowed to reach room temperature, diluted with Et2O, decomposed with saturated aqueous NH4Cl, the organic layer separated, washed with H2O, dried, evaporated, and the residue chromatographed in CHCl3 on Al2O3 gave 2 g. 2-(3,4,6,7-tetramethoxy-9- phenanthrylmethyl)pyrrole (IX), m. 155-6° (C6H6-petr. ether). IX (0.4 g.) in 30 ml. AcOH containing 0.25 g. PtO2 hydrogenated 8 hrs. at room temperature at 60 lb./sq, in., filtered, the filtrate evaporated in vacuo, the residue extracted repeatedly with hot dilute HCl, the combined exts. basified with aqueous NH3, and the product isolated with CHCl3 gave 0.25 g. corresponding pyrrolidine (X), oil; picrate m. 247-9° (AcOH). X (0.5 g.) and 3 ml. 98% HCO2H heated 1.5 hrs. at 180°, cooled, dissolved in CHCl3, the solution washed, dried, evaporated, the residual N-formyl derivative refluxed 1.5 hrs. with 4 ml. POCl3 and 15 ml. PhMe, the solution mixture cooled, diluted with petr. ether, the resulting quaternary chloride dried in vacuo, reduced with 0.8 g. NaBH4 in 30 ml. MeOH, the solution evaporated in vacuo, the residue taken up in CHCl3, the solution washed with H2O, dried, evaporated, and the residue chromatographed in CHCl3 on Al2O3 gave 0.2 g. (±)-V, m. 219-21° (CHCl3-MeOH). (±)-V (200 mg.) in 10 ml. CHCl3 refluxed 3 hrs. on a H2O bath with 2 ml. MeI and kept overnight at 30°, the solution evaporated, the resulting (±)-V.MeI shaken 5 hrs. with Ag2O (from 1 g. AgNO3) and 10 ml. H2O, and the (±)-V.MeOH subjected to Hofmann degradation as above gave 40 mg. VI, m. 144.5-5.0° (C6H6-petr. ether). 2-Amino-α-(3,4- dimethoxyphenyl)-4,5-dimethoxycinnamic acid (G. et al., loc. cit.) diazotized in Me2CO with BuONO and subjected to Pschorr ring closure gave 2,3,5,6-tetramethoxyphenanthrene-9-carboxylic acid (XI). XI (5 g.) refluxed 4 hrs. with 4 ml. concentrated H2SO4 in 150 ml. MeOH gave 4.2 g. Me ester of XI, m. 150° (EtOH). XI was converted successively as above into 9-hydroxymethyl-2,3,5,6-tetramethoxyphenanthrene, m. 133° (C6H6); 9 - chloromethyl - 2,3,5,6 - tetramethoxyphenanthrene, m. 163-4° (C6H6-petr. ether); 2-(2,3,5,6-tetramethoxy-9- phenanthrylmethyl)pyrrolidine [picrate m. 218° (decomposition) (AcOH-EtOH)]; and finally 9,11,12,13,13a, 14-hexahydro3,4,6,7- tetramethoxydibenzo [f,h] pyrrolo [1,2-b] isoquinoline (XII), m. 219° (CHCl-MeOH). XII (200 mg.) converted to the methiodide and the product subjected to the Hofmann degradation as above gave 30 mg. XIII, m. 137-8° (C6H6-petr. ether). The structure of V is shown.

IT **94689-49-3P**, Xanthine, 3-isopentyl-2-thio-
RL: PREP (Preparation)
(preparation of)

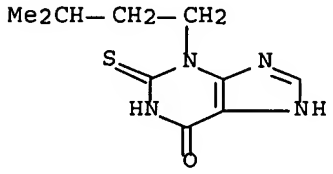
RN 94689-49-3 CAPLUS

CN Xanthine, 3-isopentyl-2-thio- (7CI) (CA INDEX NAME)



L9 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:410978 CAPLUS Full-text
DOCUMENT NUMBER: 57:10978
ORIGINAL REFERENCE NO.: 57:2268g

TITLE: Synthesis of Dihydrotriacanthine
AUTHOR(S): Leonard, Nelson J.; Laursen, Richard A.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of Organic Chemistry (1962), 27, 1778-80
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB 3-Isopentyladenine was synthesized and shown to be identical with dihydrotriacan thine.
IT **94689-49-3P**, Xanthine, 3-isopentyl-2-thio-
RL: PREP (Preparation)
(preparation of)
RN 94689-49-3 CAPLUS
CN Xanthine, 3-isopentyl-2-thio- (7CI) (CA INDEX NAME)



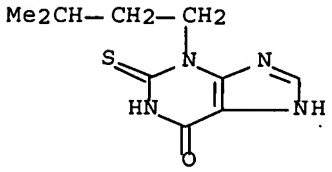
L9 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:410977 CAPLUS Full-text
DOCUMENT NUMBER: 57:10977
ORIGINAL REFERENCE NO.: 57:2267f-i,2268f-g
TITLE: Synthesis of calycotomine and its analogs
AUTHOR(S): Chatterjee, A.; Chaudhury, N. Aditya
CORPORATE SOURCE: Univ. Coll. Sci., Calcutta
SOURCE: Journal of Organic Chemistry (1962), 27, 309-10
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB cf. CA 54, 22693g. Liquid NH3 (300 ml.) containing 8.73 g. Na treated with a thin stream of 22.0 g. 3,4-(MeO)2C6H3CH2CH2NH2 and the mixture kept 6 hrs. with rise of temperature to 30° decompd, by cautious addition of ice and washed twice with 50 ml. Et2O, the aqueous phase aerated and the NH3-free solo. acidified with AcOH with cooling, washed with Et2O and made alkaline with NaHCO3, extracted 3 times with 100 ml. BuOH and the dried extract (150 ml.) treated with HCl in Et2O yielded 18.0 g. 3,4-HO(MeO)C6H3CH2CH2NH2.HCl (I), m. 203-4° (absolute alc.Et2O). I (0.9 g.) and 0.4 g. HOCH2CHO in 10 ml. H2O adjusted to pH 4.,5-5.0 and kept 3 days at 30° basified with Na2CO3 and extracted with CHCI3 gave 0.6 g. 6-demethylcalycotomine (II, R1 = OH, R2 = OMe) (III), m. 198-200° (decomposition). III (0.6 g.) in 50 ml. dry Et2O added slowly to CH2N2 [from Me(NO)NCONH2] and kept 16 hrs. at 28-6° before evapn, in vacuo, the residue (0.5 g.) taken up in 20 ml. 4N HCl and washed 3 times with 25 ml. Et2O, the acidic aqueous solution basified with 45 ml. 10% aqueous NaOH and extracted 3 times with 50 ml. CHCl3 yielded 45-50% dl-calycotomine (II, R1 = R2 - OMe), m. 134° (1:1 EtOAc-petr. ether), λ 240, 290 mμ (log ε 3.48, 3.66, alc.); HCl salt m. 195-6° (absolute alc.-Et2O). Concentrated HCl (8 ml.) heated 8 hrs. with 5.0 g. 3,4-(MeO)2C6H3CH2CH2NH2 at 160-70° in a sealed tube and the product cooled in an ice bath yielded 4.0 g.

3,4-(HO)2C6H3CH2NH2HCl (IV), m. 241° (Me2CO). IV (1.0 g.) and 0.6 g. HOCH2CHO in 10 ml. H2O adjusted to pH 3-4 and kept 3 days at 25-6°, concd, in vacuo and the cryst, product recrystd, from 1: 1 alc.-Me2CO gave 0.85 g. 6,7-demethylcalycotomine (II, R1 = R2 = OH), m. 208-9° (decomposition), λ 288 mμ (log ε 3.57). Condensation of 0.08 g. with 0.15 g. 3,4-(HO)2C6H3CH2CH(NH2)CO2H.HCl in 5 ml. H2O at pH 4-5 gave 0.1 g. 3-carboxy-6,7-demethylealycotomine, m. 281-2° (decomposition), λ 280 mμ (log ε 3.54).

IT **94689-49-3P**, Xanthine, 3-isopentyl-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 94689-49-3 CAPLUS

CN Xanthine, 3-isopentyl-2-thio- (7CI) (CA INDEX NAME)



L9 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:25096 CAPLUS Full-text

DOCUMENT NUMBER: 56:25096

ORIGINAL REFERENCE NO.: 56:4762b-h

TITLE: Synthesis and properties of 3-methylpurines

AUTHOR(S): Bergmann, Felix; Levin, Gershon; Kalmus, Abraham; Kwietny, Hanna

CORPORATE SOURCE: Hebrew Univ.-Hadassah Med. School, Jerusalem, Israel

SOURCE: Journal of Organic Chemistry (1961), 26, 1504-8
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

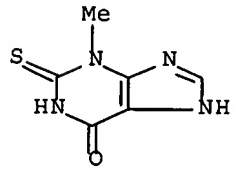
AB A series of substituted purines was prepared and, by comparison of their ultraviolet spectra, it was deduced that 3-methylhypoxanthine (I), 8-hydroxy-3-methyl-6-purinone (II), 3-methyl-8 hydroxypurine (III), 3-methylpurine-6-thione (IV), and 3-methyl-6-methylthiopurine (V) had C:N bonds fixed in the 1,2-position. This bond fixation alone was inadequate in explaining the rate of attack of these compds. by milk xanthine oxidase. 3-Methylxanthine (3 g.) was refluxed 2 hrs. with 15 g. P2S5 in 150 ml. C5H5N, the solvent evaporated, the residue heated with water (15 min.), and the pH brought to 9 with NH4OH. After 30 min., this solution was filtered, and the filtrate concentrated in vacuo to 50 ml. and acidified to pH 5.5 to precipitate 2.2 g. 2-hydroxy-3-methylpurine-6-thione (VI), which was purified by treatment with C in 5% NaOH, precipitated with HOAc, and recrystd. from water as yellow needles, decomposing above 300°. VI (1.2 g.) in 25 ml. N NaOH was refluxed 2 hrs. with 4 g. Raney Ni (VII), VII removed, and the solution evaporated to dryness. The residue was dissolved in 5% ethanolic H2SO4 and water added to just clarify the solution which, after treatment with C and storage at 0°, deposited 23% 3-methyl-2-purinone (VIII) as the sulfate in large colorless plates. VIII, colorless needles, decomposed 297-300° (EtOH). Similarly, 0.2 g. 3-methyl-6-thiouric acid refluxed 70 min. with 0.8 g. VII in 20 ml. 5% NH4OH gave, on acidification and cooling, 90 mg. 8-hydroxy-3-methyl-2- purinone, flat rods, decomposing above 300° (water). 1,2-Dihydro-1-methyl-2-thio-4-hydroxy-5,6-

diaminopyrimidine (IX) (CA 55, 2656g) (3.3 g.) and 12 ml. HCONH2 heated 1.5 hrs. at 180-90° gave, on cooling, 3.2 g. 6-hydroxy-3-methylpurine-2-thione (X), prisms, decomposing above 300° (water). X (3 g.) was heated to 90° in 70 ml. 5% NH4OH, 9 g. VII added, and heating and stirring continued 2 hrs. to give, on cooling and concentration of the solution, 1.9 g. I, colorless needles, decomposing above 300° (50% EtOH) (crystallizing with 1/3 H2O). Heating 1 g. IX and 1 g. CO(NH2)2 20 min. at 195°, dissolving the product in 5% NaOH, treating with C, and acidifying with 20% H2SO4pptd. 90% 6,8-dihydroxy-3-methylpurine-2-thione (XI), decomposing above 300°. Desulfurization of XI in 10 ml. N NaOH (refluxed 1.5 hrs. with 1.5 g. VII) followed by acidification with 20% H2SO4 gave 0.3 g. II, colorless plates, decomposing above 300° (H2O). 2,6-Dimercapto-3-methyl-8-purinol (1 g.) in 10 ml. 2.5% NaOH was refluxed with stirring with 2 g. VII; after 45 min., 2 g. VII was added and refluxing continued 70 min. The filtrate was brought to pH 7.5 with HOAc, evaporated to dryness, and the residue extracted with cold EtOH. The residue was crystallized from hot 90% EtOH to give 250 mg. III, subliming about 250°, m. above 300°. Treatment of 0.8 g. XI with 2.5 g. P2S5 in 45 ml. C5H5N (as in the preparation of VI) gave 68% 2-mercapto-3-methylpurine-6-thione (XII), yellowish elongated prisms, decomposing above 300° (Me2NCHO-water). Refluxing 1.1 g. I with 5 g. P2S5 in 60 ml. C5H5N 4 hrs. gave, after evaporation of solvent and treatment with hot water, 0.8 g. IV, yellowish pointed prisms, decomposing above 300° (H2O). Treatment of 0.4 g. IV in 5 ml. 2.5% NaOH at room temperature with 0.3 ml. MeI (2 hrs.) gave 0.4 g. V, colorless prisms (water), m. 166°. IV, V, and XII could not be desulfurized to 3-methylpurine.

IT **28139-02-8P**, Xanthine, 3-methyl-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



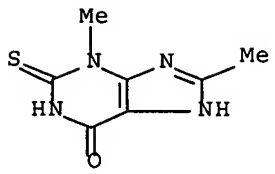
L9 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:18329 CAPLUS Full-text
DOCUMENT NUMBER: 56:18329
ORIGINAL REFERENCE NO.: 56:3480c-i,3481a-b
TITLE: Synthesis of 8-substituted purines
AUTHOR(S): Bergmann, F.; Tamari, M.
CORPORATE SOURCE: Hebrew Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society (1961) 4468-72
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 56:18329
ED Entered STN: 22 Apr 2001
AB Condensation of an acetamidine salt with an appropriate derivative of 4,5-diaminopyrimidine in the absence of a solvent led directly to high yields of

the 8-substituted purines (I). General procedure. A mixture of a 4,5diaminopyrimidine and 2 equivs. MeC(:NH)NH2.HCl (II.HCl) heated to 180-90° (homogeneous melt was formed and NH3 was evolved), when reaction ceased, the melt dissolved in N NaOH, the solution decolorized with C, and acidified with AcOH to pH 6 gave the I, all decomposing above 310° [substituents at 2-, 6-, and 8-position, reaction time in min., % yield, λ (mμ) at pH 8.0, Rf in 85:10:5 95% EtOH-H2OAcOH (solvent A), 70:20:10 95% EtOH-pyridine-H2O (solvent B), and 65:25:10 iso-PrOH-HCONMe2-10% aqueous NH3 (solvent C) given]: H, OH, Me, 60, 56 (the yield was improved by addition of 2 equivs. anhydrous NaOAc), 2.52, 0.57, 0.70, --; H, OH, Me, 60, 67 (with II.AcOH), --, --, --, --; OH, OH, Me, 30, 94, 240 and 275, 0.54, 0.60, 0.42; OH, SH, Me (III), 35, 83 (the yield was improved by addition of 2 equivs. anhydrous NaOAc) (the same compound was also prepared in 90% yield from 8-methylxanthine with P2S5), 251 and 344, 0.50, 0.56, 0.57; SH, OH, Me, 30, 77, 235 and 280, 0.45, 0.74, 0.61; SH, SH, Me, 25, 65 (the yield was improved with 2 equivs. anhydrous NaOAc), 247 and 285, and 351, 0.53, 0.59, 0.71; SH, SH, Me (IV), 25, 86 (with II.AcOH), --, --, --, --; SH, NH2, Me (V), 30, 66 (isolated as the sulfate), 230 and 251, and 280, 0.61, 0.67, --; H, OH, Ph, 70, 50, 291, 0.58, 0.79, --; H, OH, Ph, 70, 78 (with II.AcOH), --, --, --; OH, OH, Ph, 40, 80, 228 and 309, 0.52, 0.66, --. Also were prepared 92% 3,8-dimethylxanthine (VI), λ (pH 8.0) 275 m, Rf 0.64 (in A), 0.79 (in B), and 0.68 (in C), and 88% 3,8-dimethyl-2-mercaptoxanthine (VII), λ (pH 8.0), 233 and 288 mμ, Rf 0.60 (in A) and 0.84 (in B). N:C(OH).-N:C(NH2).C(NH2):CH (VIII) (Kalmus and Bergmann, CA 55, 12418h) (1 g.), 1 g. II.HCl, and 0.8 g. anhydrous NaOAc heated 20 min. at 140-5, the resulting cake dissolved in 10% aqueous NH3, the solution boiled with C, filtered, and the filtrate kept 24 hrs. in a cold room gave 0.65 g. inseparable mixture of VIII and 2-hydroxy-8-methylpurine (IX), (pH 8.0) 307 m. III (5 g.) and 1.5 g. (wet weight) Raney Ni in 25 ml. 5% aqueous NH3 refluxed 80 min., filtered, the filtrate adjusted to pH 2 with HNO3, and kept 2 months at room temperature gave IX.HNO3. If the above ammoniacal solution was acidified with H2SO4, IX decomposed quant. The same result was obtained when an ammoniacal solution of IX was evaporated to dryness, the residue extracted with absolute EtOH, and the mixture acidified with 1% alc.-H2SO4. V (580 mg.) and 1.5 g. (wet weight) Raney Ni in 100 ml. 5% aqueous NH2 refluxed 2 hrs., filtered hot, and the filtrate cooled gave 300 mg. 8-methyladenine, Rf 0.57 (in A), 0.67 (in B), and 0.64 (in C). 8-Methylhypoxanthine (1.3 g.), 5 g. P2S5, and 50 ml. dry pyridine refluxed 4 hrs., concentrated in vacuo, the residue extracted with 37 NaOH, filtered, the solution concentrated in vacuo, and kept overnight at 0° gave 1.1 g. 6-mercapto-8-methylpurine, decomposed above 310° (H2O), (pH 8.0) 232 and 316 m, Rf 0.64 (in A) and 0.71 (in C). VII (1 g.) and 0.7 ml. MeI stirred 30 min. at room temperature in 10 ml. 0.5N NaOH gave 0.95 g. 3,8-dimethyl2-(methylthio)hypoxanthine, decomposed at 312-15° (H2O), Rf 0.73 (in B). VII (2 g.) and 6 g. (wet weight) Raney Ni in 50 ml. 5% aqueous NH3 refluxed 2 hrs., filtered, and concentrated in vacuo gave 1.4 g. 3,8-dimethylhypoxanthine, decomposed at 300° (EtOH), Rf 0.6 (in B). NH.CO.NMe.C(NH2):C- (NH2).CS (X) and II.HCl or II.AcOH heated at 150-200° gave only X and tars. VI treated with P2S5 in pyridine, concentrated in vacuo, the residue decomposed with cold dilute aqueous NH3, the mixture filtered, and the filtrate adjusted to pH 6 with AcOH gave only X, λ (pH 8.0) 249 and 344 mμ, Rf 0.33 (in A). IV (1 g.) and 2.5 g. Raney Ni in 50 ml. 5% aqueous NH3 refluxed 70 min., filtered, the filtrate concentrated in vacuo, and kept overnight gave 150 mg. 8-methylpurine, λ (pH 8.0) 266 mμ, Rf 0.75 (in A).

IT **91725-06-3P**, Xanthine, 3,8-dimethyl-2-thio-
RL: PREP (Preparation)
(preparation of)

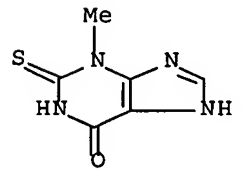
RN 91725-06-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1959:34829 CAPLUS Full-text
DOCUMENT NUMBER: 53:34829
ORIGINAL REFERENCE NO.: 53:6243f-i,6244a-c
TITLE: Some new N-methylpurines
AUTHOR(S): Elion, Gertrude B.
CORPORATE SOURCE: Wellcome Research Labs., Tuckahoe, NY
SOURCE: Ciba Foundation Symposium, Chem. and Biol. Purines (1957) 39-49
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB Ring closure in 5-formamido-4-amino-3-methyl-2-mercapto-6-oxopyrimidine (I) gave 2-mercapto-3-methylhypoxanthine (II), which on treatment with Raney Ni provided 3-methylhypoxanthine (III). I with Raney Ni gave 5-formamido-4-amino-3-methyl-6-oxopyrimidine which underwent ring closure with formamide to form III. III with P2S5 in pyridine provided 3-methyl-6-mercaptopurine which when treated with NH4OH at 140° for 16 h. gave 3-methyladenine (IV). Excellent yields of IV were obtained by treatment of II with P2S5 to form 3-methyl-2,6-dithiopurine, which was then converted to the 6-amino derivative and treated with Raney Ni to give IV. Methylation of 5-formamido-4-amino-2-mercapto-6-oxopyrimidine (V) with Me2SO4 in aqueous alkali gave the 2-methylthio-1-Me derivative (VI), as well as a water-soluble compound believed to be 4-amino-5-formamido-2-methylthio-6- methoxypyrimidine. VI with Raney Ni gave 5-formamido-4-amino-1-methyl-6- oxopyrimidine, which was converted to 1-methylhypoxanthine (VII) by heating with HCO2H. Treatment of VII with P2S5 in Tetralin or pyridine gave 1-methyl-6-mercaptopurine (VIII). Cyclization of VI with HCO2H gave 2-methylthio-1-methylhypoxanthine, which yielded 1-methylxanthine on acid hydrolysis and 1-methylguanine on heating with NH4OH. Heating of VIII with aqueous NH3 at 140° gave 4-amino-5-imidazolecarboxamide. With alc. NH3 at 160°, VIII was converted to 6-(methylamino)purine. VI with P2S5 in pyridine gave 2-methylthio-1-methyl-6-thiopurine, which when heated with NH4OH at 140° formed 1-methyl-2,6-diaminopurine. When 6-chloropurine was methylated and then treated with NaSH, 7-methyl- and 9-methyl-6-mercaptopurines were formed. These were easily separated because of a difference in solubility in water. 9-Methyladenine, prepared from 6-amino-2-methylthio-9-methylpurine, gave 9-methylhypoxanthine on treatment with HNO2. The UV absorption maximum (in mμ) at pH 1, 3, 7, and 11 were, for substituted hypoxanthines were (substituent given): H, 248, -, 249, 258; 1-Me, 249, -, 251, 260; 3-Me, 253, 262, 264, 265; 7-Me, 250, 255, 256, 262; 9-Me, 250, -, 250, 254. For substituted purines: 6-MeO, 254, -, 252, 261; 6-HS, 325, 323, 322, 233 (312); 1,6-Me(HS), 229(321), 233(321), 235(320), 237(321); 3,6-Me(HS), 244(334), 245(340), 245(337), 245(332); 7,6-Me(HS), 328, 328, 327, 234(315); 9,6-Me(HS), 323, 321, 320, 234(309); 6-MeS, 294, 290, 290, 290. At pH 1 and 11 for substituted adenines: H, 263, 267; 3-Me, 274, 273; 7-Me, 272, 271; 9-Me, 261, 262. 6-Methylaminopurine: 267, 272, at pH 1 and 11.
IT **28139-02-8P**, Xanthine, 3-methyl-2-thio-

RL: PREP (Preparation)
(preparation of)
RN 28139-02-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



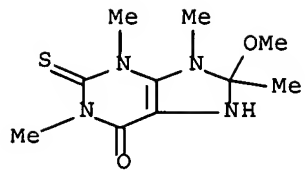
L9 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:16071 CAPLUS Full-text
DOCUMENT NUMBER: 49:16071
ORIGINAL REFERENCE NO.: 49:3204a-i,3205a-c
TITLE: Syntheses in the purine series. III. Reactions of the acetates of 4,5-diaminouracil; the syntheses of caffeine, theobromine, and theophylline
AUTHOR(S): Bredereck, Hellmut; Hennig, Ingeborg; Pfleiderer, Wolfgang; Weber, Gerhard
CORPORATE SOURCE: Tech. Hochschule, Stuttgart, Germany
SOURCE: Chemische Berichte (1953), 86, 333-51
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 49:16071
ED Entered STN: 22 Apr 2001
GI For diagram(s), see printed CA Issue.
AB IIIa (20 g.) was saponified 15 min. with 120 cc. 2N NaOH, and methylated 0.5 h. at 40° with 16 cc. Me2SO4 in 14 cc. Me2CO giving, at 0° and pH 7.5. 90% [OC.NH.CO.NMe.C(NH2):CNHAc.2H2O (VI), m. 303° (from H2O). IV could be isolated as an intermediate and subsequently methylated to VI. IIIa (10 g.) refluxed with 60 cc. 2N NaOH, decolorized, cooled to 40° and treated gradually with 19 cc. Me2SO4 and 12 cc. Me2CO, maintaining pH 9 by dropwise addition of about 50 cc. 2N NaOH, over a 2-h. period. Subsequently the pH dropped to 7.5-8, and the mixture evaporated to 1/2 volume was kept 16 h. at 0° filtered from OC.NMe.CO.NMe.C(NH2): C NHAc (VII) and extracted with CHCl3 over a 30-h. period, the extraction being interrupted after 8 h., allowed to stand, filtered from precipitated VII, and the extraction continued with fresh CHCl3. Total VII, 6-7 g., m. 281° (from CHCl3. Methylating VI in KOH at 40° with EtOH and Me2SO4, yielded 80-90% VII. VI (10 g.) methylated in 2N NaOH at pH 9-10° the solution concentrated to 1/2 volume and extracted with CHCl3 (as above), and the filtrates concentrated yielded 2 g. 4-Me derivative of VII, m. 247°. Further concentration of the CHCl3 exts. gave a gummy residue yielding, when triturated with small amts. of Me2CO,OC.NMe.CO.NMe.C(NHMe):CNMeAc, prisms, m. 225° (from EtOH). IIIa (5 g.) was converted into the Na salt of IIIb which, in 60 cc. H2O was methylated 45 min. with 12 cc. Me2SO4 and 15 cc. Me2CO, evaporated to 2/3 volume, and extracted 6 h. with CHCl3 giving 1.5 g. OC.NMe.CO.NMe.C:C.NAc.CMe(OH).NH (VIII), m. 209° (from EtOH). IIIa (20 g.) saponified, and the product methylated with 105 cc. Me2SO4 at 40°, with the pH kept at 8-9 with 4N NaOH, concentrated to 1/2 volume and extracted 8 h. with CHCl3 gave 10 g. OC.NMe.CO.NMe.C:C.NAc.CMe(OMe).NMe, m. 225° (from EtOH), also

formed in 60% yield from VIII by methylation at 40° and pH 7-8. VI (3 g.) refluxed 5 h. with 5 cc. Ac2O and 5 cc. pyridine yielded 2 g. 3,8-dimethylxanthine. VII (5.2 g.) refluxed 3-5 min. with 150 cc. Ac2O gave 4.8 g. OC.NMe.CO.NMe.C(NHAc):CNHAc (IX) (isomeric with VIII), hexagons, m. 235°, resolidifying at 250° to form 1,3,8-trimethylxanthine (X), m. 325°. By heating VII, IX, or VIII with Ac2O and pyridine, recrystg. the products from H2O and heating them above their m.ps. (about 215°) X was obtained, m. 325-30° (after sublimation). The 4-Me derivative of VII (1 g.) refluxed 6 h. with 20 cc. Ac2O and 10 cc. pyridine gave 8-acetoxy-1,3,8,9-tetramethyl-7-acetyl-1,2,3,6,8,9-hexahydropurine, m. 180° (from EtOH). I sulfate (2 g.) in EtCONH2 refluxed 20 min., followed by addition of 40 cc. EtOH gave 1.9 g. (crude) 4-amino-5- propionamidouracil (XI), having no characteristic m.p., 1 g. of which heated with HCONH2 gave 0.6 g. xanthine; the latter was also formed in high yield by heating either 5-formamido-4-aminouracil (XII) or IV in HCONH2. V (5 g.), brown powder, was formed by refluxing 10 g. I sulfate in 100 g. AcNH2. V was also prepared by refluxing XII, XI, or IV with AcNH2, and if any contaminating acyl derivs. were present, they were removed by refluxing with p-MeC6H4SO3H in MeOH. I sulfate (10 g.) refluxed 8 h. with EtCONH2, cooled to 60°, and extracted with MeOH gave 7 g. 8-ethylxanthine (XIII), which methylated at pH 8-9 and 40°, with Me2SO4 gave 8-ethylcaffeine, m. 184° (from EtOH). XIII was also formed by protracted heating of IV, XI, or XII in EtCONH2. Any adhering acyl derivs. were removed as above indicated. By refluxing VI 1 h. with 7.5 parts HCONH2, extracting with dilute NH4OH and precipitating with AcOH, 5 g. 3-methylxanthine (XIV) was obtained. XIV (10 g.) warmed at 100° with 80 cc. H2O and 35 cc. 2N NaOH, followed by methylating at pH 7-7.5 and 40° with 8.7 cc. Me2SO4 and 50 cc. MeOH, followed by direct crystallization at 0° and subsequent CHCl3 extraction gave 7-7.5 g. theophylline, m. 269° the latter was also formed by converting IIIa into crude VII and (without further purification) heating with HCONH2. The 4-Me derivative of VII (3 g.) refluxed 30 min. with 15 cc. HCONH2 gave 2 g. 1,3,8,9-tetramethylxanthine (XV), m. 254° (from EtOH), and, from the mother liquor from XV, after adding H2O and extracting with CHCl3 was obtained 1,3,9-trimethylxanthine (isocaffeine), m. 282-5° (from CHCl3, after trituration with Me2CO). XV was also formed by refluxing the 4-Me derivative of VII with AcNH2. VI (10 g.) refluxed 3 h. with MeOH containing 10-15% HCl gave the HCl salt of 4,5-diamino-3-methyluracil (XVI), yielding 6.2 g. of the free base with NH4OH. VII (10 g.) with MeOH-HCl as above gave the HCl salt of the 1-Me derivative of XVI, yielding 4.8 g. of the free base, m. 208-10°. VI (3 g.) refluxed 30 min. with 2N NaOH and acidified with 2N H2SO4 gave 2 g. 3,8-dimethylxanthine, needles, readily methylated to 1,3,7,8-tetramethylxanthine, m. 207-8° (from H2O). VII (3 g.) refluxed 1.5 h. with 60 cc. 0.3N NaOH and extracted with CHCl3 gave X, similarly obtained from VIII or IX. 8-Methoxy-2,6-dioxo-1,3,8,9- tetramethyl-7-acetyl-1,2,3,6,8,9-hexahydropurine (4 g.) refluxed 0.5 h. with 0.3N NaOH and extracted with CHCl3 gave the compound C10H16O3N4, m. 246° (probably OC.NMe. CO.NMe.C:C.NH.CMe(OMe).NMe), the structure of which was not proved.

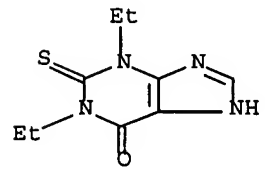
IT **841313-24-4P**, Xanthine, 8,9-dihydro-8-methoxy-1,3,8,9-tetramethyl-
RL: PREP (Preparation)
(preparation of)

RN 841313-24-4 CAPLUS

CN Xanthine, 8,9-dihydro-8-methoxy-1,3,8,9-tetramethyl- (5CI) (CA INDEX NAME)

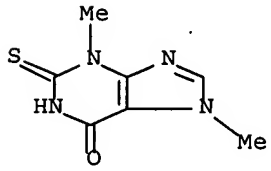


L9 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1951:61193 CAPLUS Full-text
DOCUMENT NUMBER: 45:61193
ORIGINAL REFERENCE NO.: 45:10401e-g
TITLE: Diuretic activity of compounds related to xanthines, uracils, and triazines as determined in dogs
AUTHOR(S): Kattus, Albert A.; Newman, Elliot V.; Franklin, John
CORPORATE SOURCE: Johns Hopkins Univ., Baltimore, MD
SOURCE: Bulletin of the Johns Hopkins Hospital (1951), 89, 1-8
CODEN: JHHBAI; ISSN: 0097-1383
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB A series of 19 substituted xanthines, 1 thioxanthine, 14 uracils, 1 thiouracil, 3 triazines, 2 phenothiazines, and a substituted N-benzylaniline were tested for diuretic activity in female dogs. Urine vols. and Na excretions from dogs receiving two 0.25-0.5-g. doses in 1 day were compared with those from the same dogs prior to dosing. With Na excretion as a criterion, 1,3-diethylxanthine (I), its 2-thio analog, and its 8-bromo derivative (II) were highly diuretic, but caused emesis. Emesis was also noted with other 1,3-dialkylxanthines. In human subjects I caused diuresis and vomiting, but II had neither action. Except for 1-propyl-3-ethyl-6-aminouracil, uracil derivs. were less active than the xanthine derivs. and produced less gastrointestinal disturbance; 2,4-bis(acetamido)-s-triazine produced diuresis in a human volunteer.
IT **841313-23-3**, Xanthine, 1,3-diethyl-2-thio-
(diuretic activity of)
RN 841313-23-3 CAPLUS
CN Xanthine, 1,3-diethyl-2-thio- (5CI) (CA INDEX NAME)



L9 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1931:52428 CAPLUS Full-text
DOCUMENT NUMBER: 25:52428
ORIGINAL REFERENCE NO.: 25:5894f-i
TITLE: Methylcaffeidine
AUTHOR(S): Biltz, Heinrich; Rakett, Hans

SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1931), 64B, 1970-4
CODEN: BDCBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 16 Dec 2001
GI For diagram(s), see printed CA Issue.
AB Some yrs. ago it was briefly (C. A. 22, 4477) reported that caffeidine (I) can be methylated with Me2SO4 to methylcaffeidine (II), which was characterized as a perchlorate m. 173°. Often, however, the II so obtained was not pure and further study has shown that the action of Me2SO4 on I is very slow and may easily lead to the formation of mixts. of I and II. Recourse was therefore again had to MeI, which gives an equimol. mixture of II and I.HI, readily separated by means of CHCl3. In this way pure II, m. 98-9°, is obtained in 1.6 g. yield from 3.4 g. I. the I.HI (2.6 g.) m. 247-9°, solubility about 4.4 in boiling alc. and 1.1 at room temperature Salts of II: perchlorate, m. 173°; chloroaurate, lemon-yellow, very unstable; Ag nitrate, [Ag(C8H14ON4)]NO3, easily decomposed by light or by organic compds. and non-noble metals, can often, with care, be crystallized from water. Salts of I: chloroplatinate, orange; chloroaurate, wine- to brown-red, deposits Au on attempted crystallization from water; fluoborate, m. 219° (decomposition); thiocyanate, m. 197°, yields on heating 2 hrs. at 160-70° a small quantity (0.12 g. from 2 g. of the salt) of what is apparently 2-thiotheobromine, m. 298°, solubility in boiling water about 0.3. II gently warmed with MeI gives a HI salt, C9H18O2N4.HI, m. 153° (decomposition), which reacts with AgNO3 in water. II therefore has the structure N:CH.NMe.C(CONHMe:CNMe2. I fused with MeNHCONH2 or EtNHCONH2 yields theobromine; in both cases the alkylurea gives HOCN, which adds to the NHMe residue of the I (position 3 of the purine nucleus) and forms a ring by displacing the other NHMe group (position 1). Similarly, fusion with CO(NHMe)2 gives caffeine, with CO(NHEt)2 1-ethyltheobromine. With PhNHCONH2 and CO(NHPh)2 there is no reaction.
IT **19373-97-8P**, Theobromine, 2-thio-
RL: PREP (Preparation)
(preparation of)
RN 19373-97-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1928:37616 CAPLUS Full-text
DOCUMENT NUMBER: 22:37616
ORIGINAL REFERENCE NO.: 22:4477c-i,4478a-e
TITLE: Caffeidine and caffeidinecarboxylic acid
AUTHOR(S): Biltz, Heinrich; Rakett, Hans
CORPORATE SOURCE: Univ. Breslau
SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1928), 61B, 1409-22

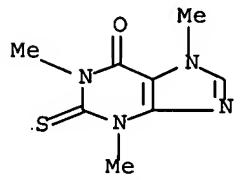
CODEN: BDCBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 16 Dec 2001
GI For diagram(s), see printed CA Issue.
AB Caffeine with alkalies takes up 1 mol. H2O to form caffeidinecarboxylic acid (I), which by loss of CO2 gives caffeidine; this, from its monobasic character and its reactions must have the structure II. Whether in the formation of I the purine ring is broken between positions 1 and 2 or 2 and 3 was not known but the present work shows that it is between 1 and 2 and hence that I has the structure III. In its preparation 2 N NaOH in moderate excess was used instead of Ba(OH)2 and heating was avoided; by shaking with a machine, the time necessary for the reaction was reduced from more than 2 weeks to 3-4 days. From the cooked solution the II can be precipitated directly with HNO3 as the difficultly soluble nitrate (hitherto described as a hygroscopic substance), and from the mother liquors that I is obtained as the Cu salt by the original May and Andreasch method. II behaves as a monoacid base (with HCl, HI, HNO3, HClO4, H2PtCl6). With H2SO4 it forms a 1:1 salt, to be sure, but this is undoubtedly an acid salt. Since caffeine is monoacid through the 9-N atom and the imidazole ring of II is the same as that in caffeine, the basic nature of II is probably due to the same N atom (3 in the notation for II). The MeNH group on C atom 4 is apparently not capable of adding acids, probably because of the adjacent 4,5-double bond. In agreement with this view is the fact that I, whose 8-N atom certainly does not add acids, forms with acids salts like caffeine and II. II also forms a complex Ag salt [Ag(C7H12ON4)2NO3] with AgNO3. The action of HNO2 on II shows that the 8-N atom is secondary. The 7-MeNH group does not react with HNO2, for allo-caffuric acid can in no way be nitrosated. Since I does not react with HNO2, the CO2H group must be on N atom 8, as shown in formula III. Similarly II can and I cannot be benzoylated. The 1st Me group which can be introduced with MeI certainly enters the same position; the 2nd Me group, which can be likewise introduced with MeI, may enter position 7 but this is not proved. Me2SO4 introduces only one Me group. The smooth transformation of II into 1,3 dimethylparabanic acid does not seem to harmonize with the structure given for II; it would appear to indicate that II contains a ring with two NMe groups. The explanation is doubtless that the reaction is complicated; the II splits open between positions 2 and 3, a CO2H group is produced at 2, and this with the NHMe group at 8 forms the new ring of the parabanic acid, the N atoms at 3 and 7 being split off by oxidation at the same time. The presence of the 4,5-double bond in II can be shown by means of Cl in MeOH and H2O; in MeOH is obtained caffeidine-4,5-glycol di-Me ether (IV), while with Cl water the II likewise adds two HO groups at the double bond but at the same time oxidation occurs at 2 and the MeNHCO group at 6 is split off, the product being 1-methyl-2-heto-1-methylaminotetrahydroimidazole-4,5-glycol (V) II can be converted back to caffeine, with 50% yield, with ClCO2Et or KOCN, and, through the amide of I, into theobromine. With CSCl2 is obtained a 2-thiocaffeine (VI), which can be converted in CHCl3 into the 8-Cl derivative (VII), and this with NaOMe gives the 8-MeO compound (VIII), which can be rearranged into 2-thiotetramethyluric acid (IX) or converted with HCl into 1,3,7-trimethyl-2-thiouric acid (X). Finally VII was converted into 1,3,7-trimethyl-2,8-dithiouric acid (XI) and, by alkylation, into various ethers of 2-thio-8-thiocaffeine (XII). Nitrate of II (yield, 41%), m. 215° (decomposition), solubility in boiling H2O about 50, H2O at room temperature about 2, boiling MeOH about 2.7, boiling AcOH about 15 (with decomposition). II, as determined by J. Pohl, has no diuretic action and does not affect the blood pressure. Perchlorate, m. 220-1° (decomposition), solubility in boiling MeOH and EtOH about 8.6; HCl salt, m. 215° (decompose), is not deliquencent when pure. Bz derivative, m. 174°, decomposed by alkalies, stable towards dilute acids, forms no salts with acids. NO derivative, m. 155° (effervescence), quite stable towards even concentrated NaOH at room temperature, forms no salts with

acids. Methylcaffeidine (3.5 g. from 5 g. II.HNO3 and alkaline Me2SO4), m. 86° perchlorate, m. 173°, solubility in MeOH at room temperature 1.8, at the b. p. about 8. IV.HCl (2.5 g. from 5 g. II in cold dry alc. with Cl); free IV, m. 164°. V.HCl, crystals with 1 H2O, m. 112°, belonging (according to J. Valeton) to the monoclinic holohedral class, β 116° 17', a:b:c = 1.074:1:1.480, gives (CO2H)2 when dissolved in boiling 2 N NaOH and then boiled a short time with AcOH. Free V, prepared from the HCl salt with KOCN (but not with NaOH, Na2CO3, Ba(OH)2, PbCO3 or Ag2O), m. 163° (effervescence), solubility in alc. at room temperature about 0.3, at the b. p. 1. Amide of I, from II and urea with HCl gas at 135-40°, m. 244-5°, gives theobromine on long boiling in mineral acids or AcOH, evaporation with concentrated HCl, boiling with Na2CO3 and acidifying with AcOH, treating with HCl gas in alc. or heating above its m. p. VI (20-2 g. from 25 g.JJ II. HNO3), light yellow, sinters 203°, m. 205°, soluble in concentrated mineral acids but repptd. on dilution, much more bitter than caffeine and has a strong diuretic action; perchlorate, deflagrates on Pt, m. 239-40° (decomposition), hydrolyzed by boiling H2O or alc. VII (6-7 g. from 8.6 g. VI), yellow, m. 186-7°, easily soluble in concentrated acids. VIII (1.5-1.7 g. from 2 g. VII), m. 174°, solubility in boiling alc. about 25. IX, from VIII in MeOH at 200°, darkens 260°, m. 297-8°. X, m. 343°, apparently with decomposition, soluble in alkalies and concentrated mineral acids. XI (2.5 g. from 3 g. VII with boiling aqueous KSH), yellow, m. 285°, solubility in boiling H2O about 0.8, easily soluble in alkalies and repptd. by acids; Na and K salts, yellow. Me ether of XII (0.8 g. from 1 g. XI with alkaline Me2SO4), m. 183°, solubility in alc. about 5. Et ether (0.9 g. from 1 g. XI with EtBr and KOH), light yellow, m. 156°. Allyl ether, yellow, m. 98°. I m. 159° (decomposition); AcOH compound, m. 127-9°; nitrate, m. 173° (effervescence); perchlorate, m. 167-8° (effervescence); HCl salt, m. 179° (decomposition).

IT **24049-32-9P**, Caffeine, 2-thio- **879683-47-3P**, Caffeine, 2-thio-, perchlorate
RL: PREP (Preparation)
(preparation of)

RN 24049-32-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 879683-47-3 CAPLUS

CN Caffeine, 2-thio-, perchlorate (3CI) (CA INDEX NAME)

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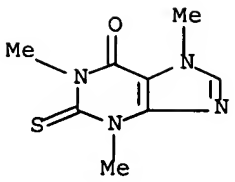
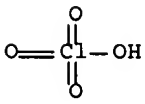
CRN 24049-32-9

CMF C8 H10 N4 O S



CM 2

CRN 7601-90-3
CMF Cl H O4



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L5          378 SEA ABB=ON  PLU=ON  HANSON S?/AU
L6            0 SEA ABB=ON  PLU=ON  NORDVAL G?/AU
L7           17 SEA ABB=ON  PLU=ON  TIDEN A?/AU
L8            1 SEA ABB=ON  PLU=ON  (L5 OR L6) AND L7

L9           47 SEA ABB=ON  PLU=ON  L4 NOT L8

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SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/13/07
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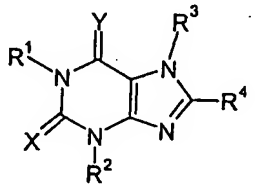
Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Date: _____ Search #2 Claim 8 +

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Some claim 9 species

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



(Ia)

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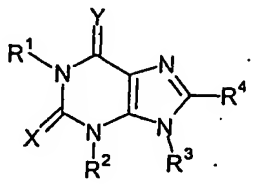
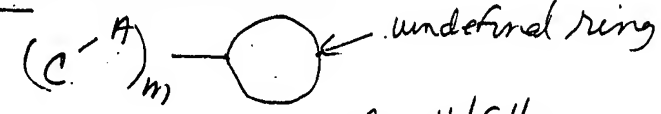


(Ib)

wherein:

X represents S, and Y represents C;

R_3, R_4, R^1 represents hydrogen or Cl to 6 alkyl;

R_2 =  ← undefined ring

m = 1-6 A = H/CH_3

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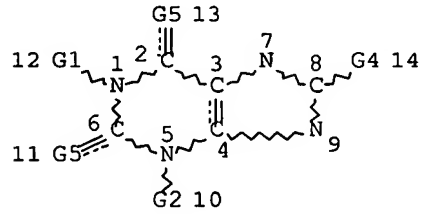

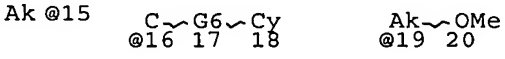

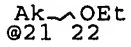


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VAR G2=16/15/OME/OET/19/21
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REP G6=(0-5) C
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CONNECT IS E2  RC AT  19
CONNECT IS E2  RC AT  21
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22
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STEREO ATTRIBUTES: NONE
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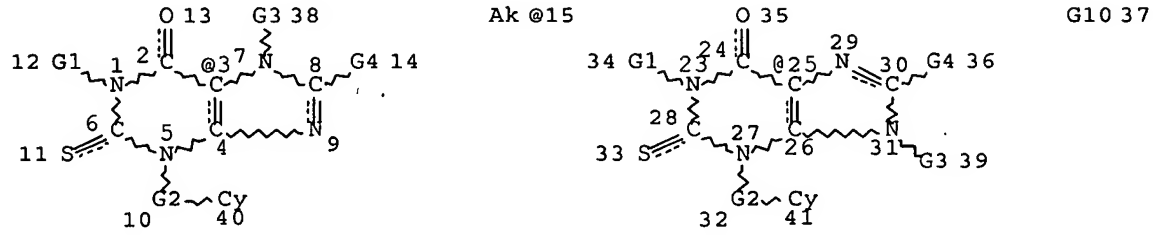

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CONNECT IS E1 RC AT 15
DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 229 ITERATIONS 17 ANSWERS
SEARCH TIME: 00.00.01

=> fil capl; s l8
FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007
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L9 8 L8

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L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089430	A1	20031030	WO 2003-SE617	20030415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480452	A1	20031030	CA 2003-2480452	20030415
AU 2003224548	A1	20031103	AU 2003-224548	20030415
EP 1499613	A1	20050126	EP 2003-721211	20030415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009012	A	20050201	BR 2003-9012	20030415
CN 1646531	A	20050727	CN 2003-808355	20030415
JP 2005526836	T	20050908	JP 2003-586151	20030415
NZ 535406	A	20060831	NZ 2003-535406	20030415
ZA 2004007815	A	20051004	ZA 2004-7815	20040928
US 2005234036	A1	20051020	US 2004-511537	20041015
NO 2004004998	A	20050118	NO 2004-4998	20041117
PRIORITY APPLN. INFO.:			SE 2002-1193 A	20020419
			SE 2002-2239 A	20020717
			WO 2003-SE617 W	20030415

OTHER SOURCE(S): MARPAT 139:350580
ED Entered STN: 31 Oct 2003
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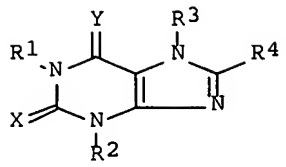

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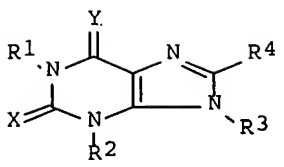
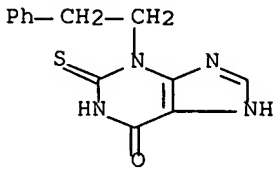


II

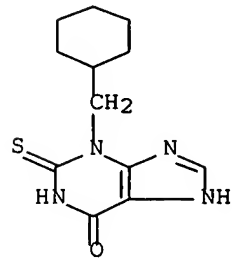
AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μM.

IT **139460-82-5P 618913-20-5P 618913-24-9P**
618913-26-1P 618913-27-2P 618913-28-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 139460-82-5 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(2-phenylethyl)-2-thioxo- (9CI) (CA INDEX NAME)

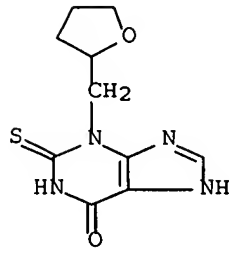


RN 618913-20-5 CAPLUS
CN 6H-Purin-6-one, 3-(cyclohexylmethyl)-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)

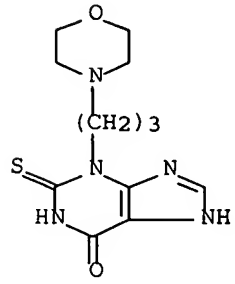


RN 618913-24-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[(tetrahydro-2-furanyl)methyl]-2-

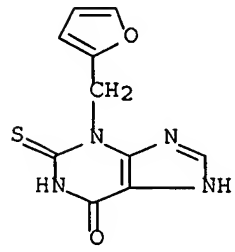
thioxo- (9CI) (CA INDEX NAME)



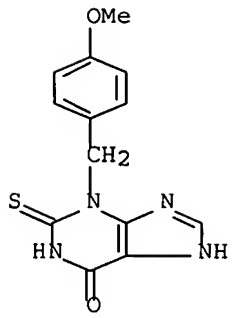
RN 618913-26-1 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-2-thioxo-
(9CI) (CA INDEX NAME)



RN 618913-27-2 CAPLUS
CN 6H-Purin-6-one, 3-(2-furanylmethyl)-1,2,3,7-tetrahydro-2-thioxo- (9CI)
(CA INDEX NAME)

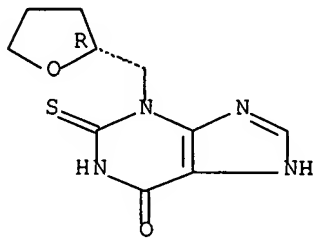


RN 618913-28-3 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[(4-methoxyphenyl)methyl]-2-thioxo-
(9CI) (CA INDEX NAME)



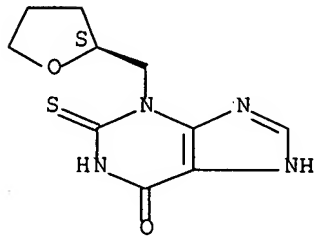
IT **618913-30-7P 618913-31-8P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)
RN 618913-30-7 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[(2R)-tetrahydro-2-furanyl]methyl]-2-thioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



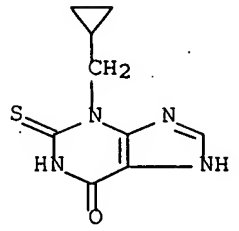
RN 618913-31-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[(2S)-tetrahydro-2-furanyl]methyl]-2-thioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

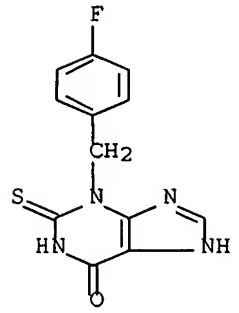


IT **618913-22-7P 618913-29-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)
RN 618913-22-7 CAPLUS

CN 6H-Purin-6-one, 3-(cyclopropylmethyl)-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



RN 618913-29-4 CAPLUS
CN 6H-Purin-6-one, 3-[(4-fluorophenyl)methyl]-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:502824 CAPLUS Full-text
DOCUMENT NUMBER: 137:63122
TITLE: Preparation of purine derivatives or therapeutic use as phosphodiesterase IV inhibitors
INVENTOR(S): Chasin, Mark; Cavalla, David J.; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 285,473. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6413975	B1	20020702	US 2000-539571	20000331
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
HU 200200938	A2	20021028	HU 2002-938	20000331
JP 2001316314	A	20011113	JP 2000-136383	20000509

US 2003073834	A1	20030417	US 2002-62280	20020201
PRIORITY APPLN. INFO.:			US 1999-285473	A2 19990402
			IN 1994-CA514	A1 19940630
			US 1997-963054	A2 19971103
			US 1997-875487	A2 19971113
			US 1998-151949	A2 19980911
			US 1998-210556	A2 19981211
			US 1998-210557	A2 19981211
			US 1999-227057	A2 19990107
			US 1999-237638	A2 19990126
			US 1999-361196	A2 19990726
			US 2000-506624	A2 20000218
			US 2000-539571	A2 20000331
			US 2000-547575	A2 20000412
			US 2000-547898	A2 20000412
			US 2000-636146	A2 20000810
			US 2000-724321	B1 20001128

OTHER SOURCE(S): MARPAT 137:63122
ED Entered STN: 04 Jul 2002
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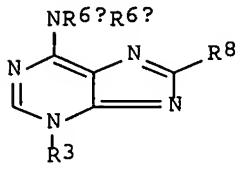

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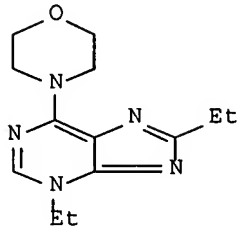


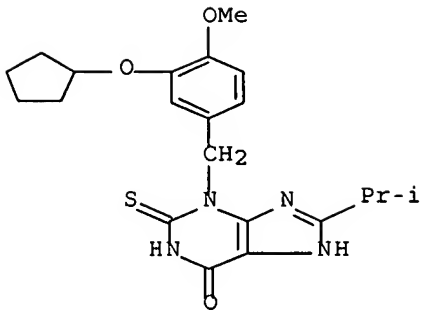
II

AB Purines, such as I [R3, R6a, R6b, R8 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase IV (PDE IV) inhibitors. Thus, 3,8-diethyl-6-morpholino- 3H-purine (II) was prepared by conversion of 3,8-diethyl-2-thioxanthine to 3,8-diethylhypoxanthine using 2N NaOH and nickel aluminum alloy, reaction of 3,8-diethylhypoxanthine to 3,8-diethyl-6-thiohypoxanthine using phosphorus pentasulfide in pyridine and, finally, reaction of 3,8-diethyl-6-thiohypoxanthine with morpholine. The prepared purine derivs. were assayed for PDE IV inhibition.

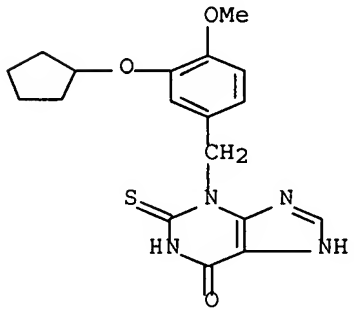
IT **300781-30-0P**, 3-(3-Cyclopentyloxy-4-methoxybenzyl)-8-isopropyl-2-thioxanthine **300781-35-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of purine derivs. for therapeutic use as phosphodiesterase IV inhibitors)

RN 300781-30-0 CAPLUS

CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 300781-35-5 CAPLUS
CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:136945 CAPLUS Full-text
DOCUMENT NUMBER: 134:193441
TITLE: Preparation of hypoxanthines and thiohypoxanthines as phosphodiesterase IV inhibitors
INVENTOR(S): Chasin, Mark; Hofer, Peter; Cavalla, David
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001011967	A1	20010222	WO 2000-US21836	20000809

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2379356	A1	20010222	CA 2000-2379356		20000809
EP 1202628	A1	20020508	EP 2000-953925		20000809
EP 1202628	B1	20041013			
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JP 2003506467	T	20030218	JP 2001-516330		20000809
AT 279113	T	20041015	AT 2000-953925		20000809
PRIORITY APPLN. INFO.:			US 1999-148623P	P	19990812
			WO 2000-US21836	W	20000809

OTHER SOURCE(S): MARPAT 134:193441
ED Entered STN: 25 Feb 2001
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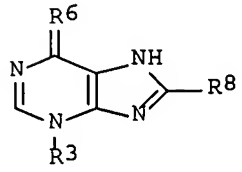

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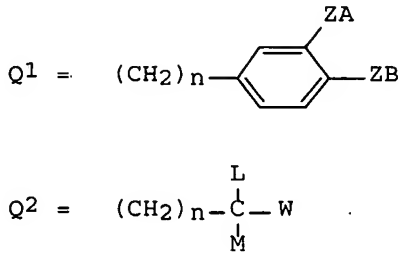
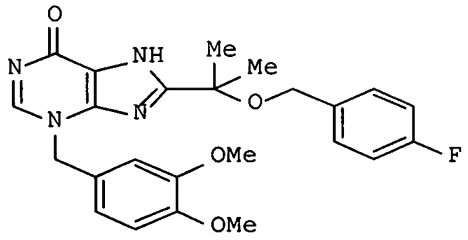


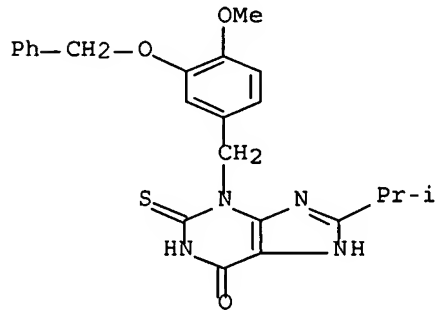


II

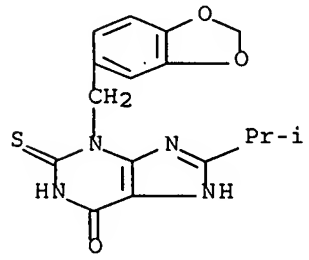
AB Title compds. (I) [wherein R3 and R8 = independently (cyclo)alkyl, alkenyl, alkynyl, Q1, or Q2; R6 = S or O; n = 0-1; Z = a bond, CH2, NH, O, or S; A and B can form a ring by adding 1-3 CH2 groups when Z = CH2, NH, O or S; and A and B are not in a ring when Z = a bond, wherein A and B = independently H, halo, (cyclo)alkyl, (cyclo)alkoxy, OH, or (un)substituted Ph, benzyl, or benzyloxy; L and M = independently H or Me; W = Q1, OH, (hetero)aryl, heterocyclyl, or (un)substituted benzyloxy] were prepared as selective phosphodiesterase (PDE) IV inhibitors. For example, amidation of 2-(4-fluorobenzyloxy)-2-methylpropionyl chloride with 5,6-diamino-1-(3,4-dimethoxybenzyl)-2-thiouracil using TEA in THF (20.4%), followed by cyclization with NaOH to form the 2-thioxanthine (79.1%) and treatment with Raney nickel in 1-propanol (67.2%), afforded the hypoxanthine (II). In assays measuring isolated PDE isoenzyme activity, II selectively inhibited PDE IV compared to PDE III and PDE V with IC50 values of 1.079 μM, 69.62 μM, and 35.80 μM, resp. As a result, I are expected to induce the desirable anti-asthmatic effects associated with PDE IV inhibition without causing the undesirable cardiovascular stimulation associated with PDE III inhibition (no data). I are useful in the treatment of asthma, allergies, inflammation, depression, dementia, and other disease states associated with abnormally high physiol. levels of cytokine (no data).

IT **227763-83-9P**, 3-(3-Benzyloxy-4-methoxybenzyl)-8-isopropyl-2-thioxanthine **327036-65-7P**, 3-(3,4-Methylenedioxybenzyl)-8-(1-methylethyl)-2-thioxanthine **327036-70-4P**, 3-(3,4-Dimethoxybenzyl)-8-(1-methylethyl)-2-thioxanthine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of hypoxanthine and thiohypoxanthine phosphodiesterase IV inhibitors from thiouracils and acyl halides and anhydrides)

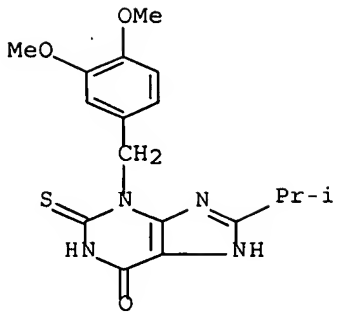
RN 227763-83-9 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[4-methoxy-3-(phenylmethoxy)phenyl]methyl]-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



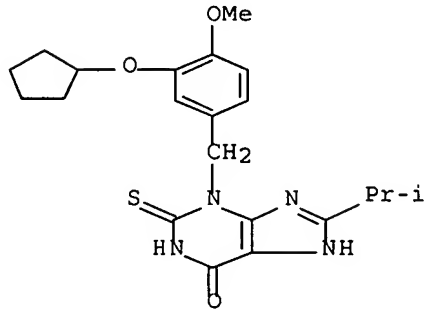
RN 327036-65-7 CAPLUS
CN 6H-Purin-6-one, 3-(1,3-benzodioxol-5-ylmethyl)-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 327036-70-4 CAPLUS
CN 6H-Purin-6-one, 3-[(3,4-dimethoxyphenyl)methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



IT **300781-30-0**, 3-(3-Cyclopentyloxy-4-methoxybenzyl)-8-isopropyl-2-thioxanthine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of hypoxanthine and thiohypoxanthine phosphodiesterase IV inhibitors from thiouracils and acyl halides and anhydrides)
RN 300781-30-0 CAPLUS
CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

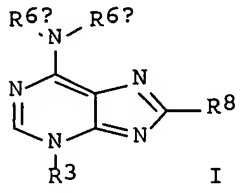
L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:725418 CAPLUS Full-text
DOCUMENT NUMBER: 133:296324
TITLE: Synthesis and phosphodiesterase IV inhibition activity of purine derivatives
INVENTOR(S): Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig, Andre; Wintergest, Peter
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059449	A2	20001012	WO 2000-US8525	20000331

WO 2000059449 A3 20010104
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

IN 180930	A1	19980404	IN 1995-CA1508		19951123
IN 181538	A1	19980711	IN 1995-CA1506		19951123
CA 2367143	A1	20001012	CA 2000-2367143		20000331
EP 1169321	A2	20020109	EP 2000-919929		20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
HU 200200938	A2	20021028	HU 2002-938		20000331
JP 2002541078	T	20021203	JP 2000-609014		20000331
BR 2000011182	A	20030610	BR 2000-11182		20000331
JP 2001316314	A	20011113	JP 2000-136383		20000509
PRIORITY APPLN. INFO.:			US 1999-285473	A	19990402
			IN 1994-CA514	A1	19940630
			WO 2000-US8525	W	20000331

OTHER SOURCE(S): MARPAT 133:296324
ED Entered STN: 13 Oct 2000
GI



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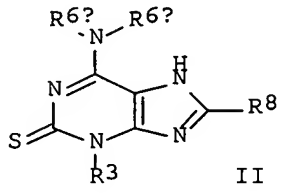
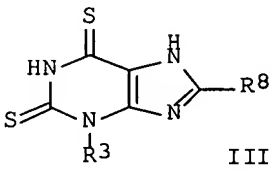


II



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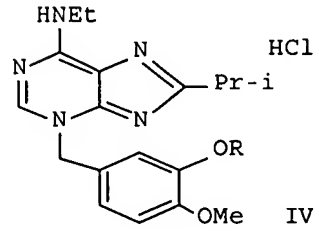
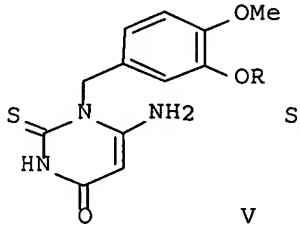
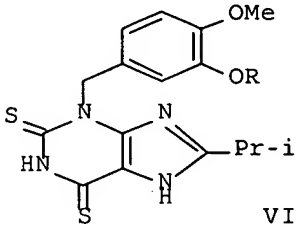


IV



V



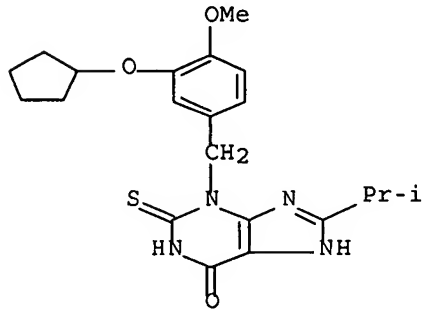
VI

AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH2)5) was prepared by etherification of isovanilline with cyclopentanol, oximation, reduction to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC50

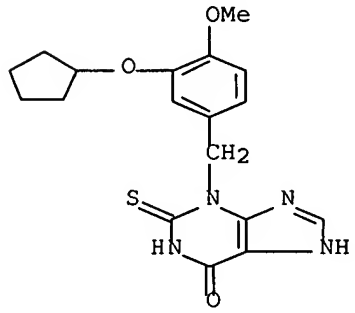
of IV against phosphodiesterase IV inhibition was 0.32 μM. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

IT **300781-30-0P 300781-35-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of purine derivs. as phosphodiesterase IV inhibitors)

RN 300781-30-0 CAPLUS
CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 300781-35-5 CAPLUS
CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)

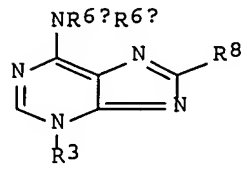


L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

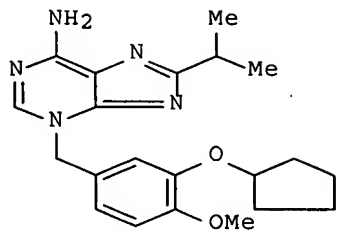
ACCESSION NUMBER:	1999:404966 CAPLUS Full-text
DOCUMENT NUMBER:	131:58700
TITLE:	Preparation of purine derivatives having phosphodiesterase IV inhibiting activity
INVENTOR(S):	Cavalla, David; Chasin, Mark; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter
PATENT ASSIGNEE(S):	Euro-Celtique, S.A., Luxembourg
SOURCE:	PCT Int. Appl., 44 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	21
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931102	A1	19990624	WO 1998-US26293	19981211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 180930	A1	19980404	IN 1995-CA1508	19951123
IN 181538	A1	19980711	IN 1995-CA1506	19951123
US 6037470	A	20000314	US 1998-209658	19981210
US 6040447	A	20000321	US 1998-209922	19981210
US 6057445	A	20000502	US 1998-209664	19981210
CA 2314335	A1	19990624	CA 1998-2314335	19981211
AU 9918159	A	19990705	AU 1999-18159	19981211
AU 747366	B2	20020516		
BR 9815171	A	20001010	BR 1998-15171	19981211
EP 1045849	A1	20001025	EP 1998-963053	19981211
EP 1045849	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TR 200001706	T2	20001121	TR 2000-200001706	19981211
US 6211367	B1	20010403	US 1998-210557	19981211
US 6228859	B1	20010508	US 1998-210556	19981211
HU 200100417	A2	20011228	HU 2001-417	19981211
HU 200100417	A3	20020429		
JP 2002508376	T	20020319	JP 2000-539025	19981211
JP 3504234	B2	20040308		
AT 244243	T	20030715	AT 1998-963053	19981211
PT 1045849	T	20031128	PT 1998-963053	19981211
ES 2202924	T3	20040401	ES 1998-963053	19981211
NO 2000002998	A	20000719	NO 2000-2998	20000609
PRIORITY APPLN. INFO.:			US 1997-69371P	P 19971212
			IN 1994-CA514	A1 19940630
			WO 1998-US26293	W 19981211

OTHER SOURCE(S): MARPAT 131:58700
ED Entered STN: 01 Jul 1999
GI



I



II

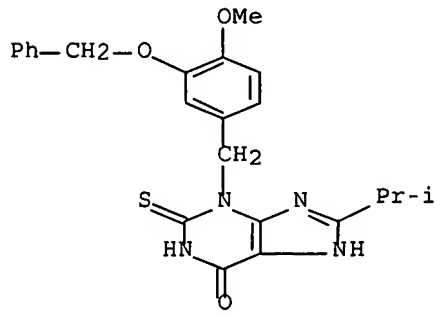
AB Purines I [R3 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, wherein said alkyl, alkenyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl; R6a, R6b = H, alkyl, alkenyl, cycloalkyl, cycloalkenyl; R8 = H, alkyl, alkenyl, cycloalkyl,

cycloalkenyl] were prepared for use as phosphodiesterase inhibitors for the treatment of diseases such as asthma, allergy, or inflammation. Thus, purine derivative II was prepared starting from 3-(3-cyclopentyloxy-4-methoxybenzyl)-8-isopropylhypoxanthine. The prepared purines were tested for inhibitory activity against phosphodiesterase types III, IV, and V.

IT **227763-83-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of purine derivs. having phosphodiesterase IV inhibition activity)

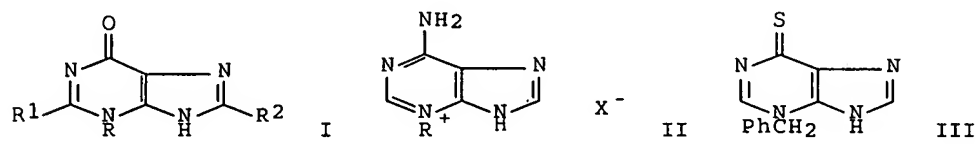
RN 227763-83-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[4-methoxy-3-(phenylmethoxy)phenyl]methyl]-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

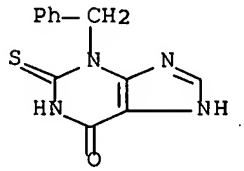
L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:214213 CAPLUS Full-text
DOCUMENT NUMBER: 116:214213
TITLE: Inhibitors of human purine nucleoside phosphorylase. Synthesis and biological activities of 8-amino-3-benzylhypoxanthine and related analogs
AUTHOR(S): Woo, Peter W. K.; Kostlan, Catherine R.; Sircar, Jagadish C.; Dong, Mi K.; Gilbertsen, Richard B.
CORPORATE SOURCE: Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(8), 1451-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:214213
ED Entered STN: 31 May 1992
GI



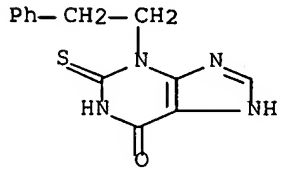
AB 3-Substituted hypoxanthines I (R = CH2Ph, CH2C6H3Cl2-3,4, CH2C6H4CN-4, CH2C6H4NO2-4, CH2C6H4OMe-4, CH2CH2Ph, 2-thienylmethyl, 2-furylmethyl; R1 = H, SMe, OH, NH2; R2 = H, NH2, NHCHO) and analogs II (R = CH2Ph, X = Cl; R = CH2C6H4NO2-4, X = Br) and III have been synthesized as inhibitors of purine nucleoside phosphorylase (PNP), which may conceivably act as T-cell-selective immunosuppressive agents with potential utility in autoimmune disorders such as rheumatoid arthritis, in organ transplantations, and in T-cell leukemias. The compds. were evaluated for their PNP activity by a radiochem. assay and also for their cytotoxic effects on a T-lymphoblastoid cell line (MOLT-4). Appropriate substitutions on 3-benzylhypoxanthine (I, R = CH2Ph, R1, R2 = H) increase potency. Variation of the 3-aryl substituents of I (R = CH2Ph, R1, R2 = H) failed to further increase potency. Replacement of the 6-oxygen function in I (R = CH2Ph, R1,R2 = H) to give II or III resulted in little change in activity. Other variations resulted in decreased activity. I (R = CH2Ph, 2-thienylmethyl, 2-furylmethyl, CH2C6H4OMe-4, R1, R2 = NH2) have moderate but significant activities, as compared to the most active inhibitor presently known, 8-amino-9-thienylguanine. I (R1, R2 = NH2) represent a novel structural type which were prepared via formation of the aminoimidazole moiety through a base-catalyzed 1,5-(O → N)-carbamimidoyl rearrangement.

IT **28741-76-6P 139460-82-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, reductive dethiolation, and purine nucleoside phosphorylase-inhibiting activity of)

RN 28741-76-6 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(phenylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)

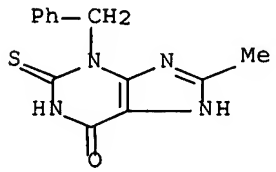


RN 139460-82-5 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(2-phenylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:105543 CAPLUS Full-text
DOCUMENT NUMBER: 84:105543
TITLE: Thermal decomposition of quaternary hypoxanthinium

salts and related purines
AUTHOR(S): Bergmann, Felix; Rahat, Miriam
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1976), (2), 239-43
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB Addnl. data considered in abstracting and indexing are available from a source cited in the original document. Thermal decomposition of quaternary hypoxanthinium salts was achieved by heating their solns. in DMF. 1,3-Dialkylhypoxanthinium bromides or iodides lost the 3-substituent as alkyl halide, which then attacked the imidazole ring at N-7 or N-9. Thermolysis of the dioxotetrahydropurinium iodide I (R = H) involved either loss of the 3-Me group as MeI giving the dihydromethylpurinedione II (R = H), or removal of HI to give the corresponding betaine which was then methylated at N-9 to give the dioxotetrahydropurinium iodide I (R = Me). The latter compound in turn decomposed to give the dimethylpurinedione II (R = Me). Similarly, the dimethylhypoxanthinium iodide III (R = H) was degraded mainly by loss of MeI, giving IV (R = H) and small amts. of V (R = H). III (R = H) also lost HI to give the corresponding betaine, which methylated at N-1 to give III (R = Me). III (R = Me) again underwent thermolysis to give a mixture of IV (R = Me) and its 9-Me isomer.
IT **59311-65-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, reduction, and NMR of)
RN 59311-65-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-8-methyl-3-(phenylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:466537 CAPLUS Full-text
DOCUMENT NUMBER: 73:66537
TITLE: N .far. N alkyl and glycosyl migration of purines and pyrimidines. III. N .far. N alkyl and glycosyl migration of purine derivatives
AUTHOR(S): Miyaki, Michiko; Shimizu, Bunji
CORPORATE SOURCE: Cent. Res. Lab., Sankyo Co., Ltd., Tokyo, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1970), 18(7), 1446-56
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 73:66537

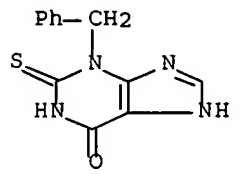
ED Entered STN: 12 May 1984

AB Alkyl and glycosyl migration reactions of N1-, N3-, N7-, and N9-substituted derivs. of adenine, N6,N6-dimethyladenine, N2-acetylguanine, and purine were demonstrated. The NMR chemical shifts of these derivs. were determined and the frontier π-electron ds. of nitrogens in purine ring calculated by a simple LCAOMO method. The results provided the order of thermodynamic stability and kinetic effect of the derivs. on the alkylation reaction.

IT **28741-76-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 28741-76-6 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(phenylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)



FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007

SEARCH HISTORY

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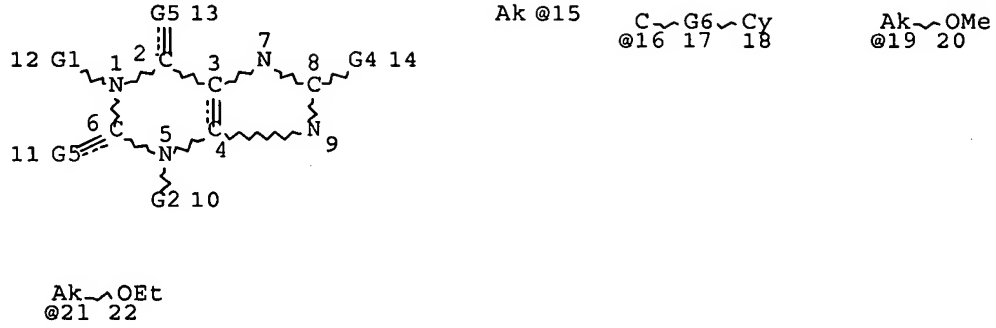
L1 STR



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VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
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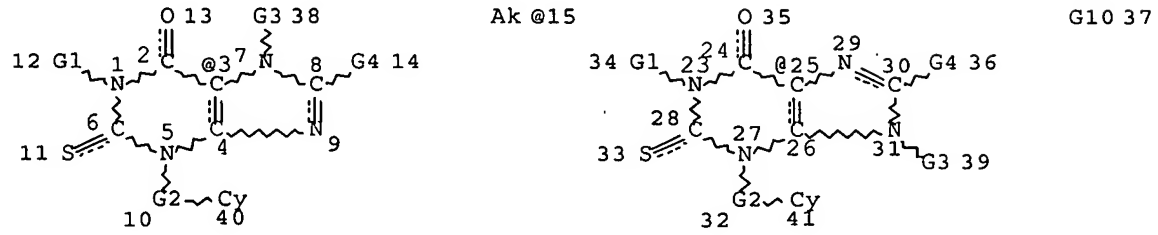
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L4 17287 SEA FILE=REGISTRY SSS FUL L1
L5 STR



VAR G1=H/15
REP G2=(1-6) C
VAR G3=H/15
VAR G4=H/15
VAR G10=3/25
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  34

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED     229 ITERATIONS                          17 ANSWERS
SEARCH TIME: 00.00.01



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L3        115605 SEA SSS FUL L1 EXTEND
L4         17287 SEA SSS FUL L1
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L5               STR L1
L6             1 SEA SUB=L4 SSS SAM L5
                 D SCAN
L7           229 SEA SUB=L4 SSS FUL L5 EXTEND
L8            17 SEA SUB=L4 SSS FUL L5
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     FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007
L9             8 SEA ABB=ON  L8
                 D IBIB ED ABS HITSTR 1-8

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